WEST Search History

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DATE: Monday, March 22, 2004

Hide?	Set Name	Query	Hit Count
	DB=USPT; PLUR=YES; OP=ADJ		
☐	L32	l31 not l10	100
☐	L31	L30 with l1	100
☐	L30	clostrid$ or neurotoxin	6508
	DB=EPAB,JPAB,DWPI; PLUR=YES; OP=ADJ		
☐	L29	L28 and l15	65
☐	L28	clostrid$ not l25	2003
	DB=PGPB; PLUR=YES; OP=ADJ		
☐	L27	US-20030166238-A1.did.	1
	DB=EPAB,JPAB,DWPI; PLUR=YES; OP=ADJ		
☐	L26	L25 and l15	25
☐	L25	neurotoxin	405
☐	L24	l20 and l21 and l22 and l23	9
☐	L23	endocyt$6 or transport$4	354269
☐	L22	cleav$ or protease or proteinase	41377
☐	L21	bind$4	389299
☐	L20	L19 or l17	11724
☐	L19	L18 with l15	161
☐	L18	"single chain"	1387
☐	L17	L16 with l15	11675
☐	L16	gene or plasmid or protein	250407
☐	L15	fus$4 or chimer$3	225808
	DB=USPT; PLUR=YES; OP=ADJ		
☐	L14	L13 same l12 same l8 not l10	2
☐	L13	l5 same (l6 or l7)	15844
☐	L12	l1 same l11	4544
☐	L11	"single chain"	10437
☐	L10	L9 and l3	25
☐	L9	l5 same l6 same l7 same l8	35
☐	L8	cleav$ or protease or proteinase	97654
☐	L7	endocyt$6	3603
☐	L6	transport$	420621
☐	L5	bind$4	338897
☐	L4	bnid$4	15

☐	L3	l1 with L2	27127
☐	L2	gene or plasmid or protein	174117
☐	L1	fus$4 or chimer$3	238926

END OF SEARCH HISTORY

09jan04 11:17:27 User208600 Session D1604.1

File 155:MEDLINE(R) 1966-2004/Jan W2 (c) format only 2004 The Dialog Corp.

Set Items Description

Ref Items RT Index-term
E1 0 1 FUSION PROTEINS, RECOMBINANT
E2 0 1 FUSION PROTEINS, VIRAL
E3 0 *FUSION PROTIEN
E4 0 1 FUSION REGULATORY PROTEIN 1, HEAVY CHAIN
E5 0 1 FUSION REGULATORY PROTEIN-1
E6 1 FUSIONA
E7 1 FUSIONABILITY
E8 6 FUSIONABLE
E9 1 FUSIONADAS
E10 1 FUSIONADO
E11 4 FUSIONADOS
E12 349 FUSIONAL

S1 39072 'RECOMBINANT FUSION PROTEINS'
S2 28703 NEUROTOX?
S3 126 S1 AND S2
S4 32438 'TOXINS'
S5 480 S1 AND S4
S6 449 S5 NOT S3
S7 328 S6 AND PY<2000
S8 133 KEX OR YSC
S9 0 S7 AND S8
S10 11 S1 AND S8

Ref Items Type RT Index-term
R1 18851 1 *PROTEASES
R2 37428 X 81 ENDOPEPTIDASES

Ref Items Type RT Index-term
R1 37428 81 *ENDOPEPTIDASES
R2 125 X DC=D8.811.277.656.300. (ENDOPEPTIDASES)
R3 0 X 1 'PEPTIDE PEPTIDOHYDROLASES
R4 18851 X 1 PROTEASES
R5 7695 X 1 PROTEINASES
R6 18978 B 107 PEPTIDE HYDROLASES
R7 777 N 3 ACROSIN
R8 433 N 10 ANCROD
R9 468 N 12 ANISTREPLASE
R10 2467 N 11 ASPARTIC ENDOPEPTIDASES
R11 385 N 11 BATROXOBIN
R12 39 N 5 BRINOLASE

S11 37428 'ENDOPEPTIDASES'
S12 9 S11 AND S7
S13 1096 S1 AND S11
S14 30746 MEMBRANE(5N) BIND?
S15 62079 TRANSLOCAT?
S16 3 S13 AND S14 AND S15
S17 72 S15 AND S13 NOT S16
S18 50 S17 NOT SECRET?
S19 28490 BOTULIN? OR TETAN?
S20 178 S1 AND S19
S21 5 S20 AND S11

Ref Items Index-term
E1 2 AU=FRANCIS ISSAC R
E2 1 AU=FRANCIS ISSAM M
E3 161 *AU=FRANCIS J
E4 2 AU=FRANCIS J A
E5 9 AU=FRANCIS J B
E6 8 AU=FRANCIS J C
E7 6 AU=FRANCIS J D
E8 51 AU=FRANCIS J E
E9 1 AU=FRANCIS J F
E10 7 AU=FRANCIS J G
E11 1 AU=FRANCIS J H
E12 5 AU=FRANCIS J J
E13 5 AU=FRANCIS J K
E14 89 AU=FRANCIS J L
E15 1 AU=FRANCIS J LYNN
E16 41 AU=FRANCIS J M
E17 4 AU=FRANCIS J N
E18 1 AU=FRANCIS J P
E19 10 AU=FRANCIS J R
E20 17 AU=FRANCIS J S
E21 4 AU=FRANCIS J T
E22 1 AU=FRANCIS J V
E23 34 AU=FRANCIS J W
E24 1 AU=FRANCIS JACKIE
E25 1 AU=FRANCIS JACQUELINE
E26 3 AU=FRANCIS JAMES
E27 3 AU=FRANCIS JAMES N
E28 2 AU=FRANCIS JANE
E29 4 AU=FRANCIS JANE M
E30 1 AU=FRANCIS JASMINE H
E31 2 AU=FRANCIS JENNELLE
E32 2 AU=FRANCIS JENNIFER
E33 1 AU=FRANCIS JENNIFER D
E34 3 AU=FRANCIS JENNIFER L
E35 1 AU=FRANCIS JEREMY S
E36 2 AU=FRANCIS JOANNA C
E37 9 AU=FRANCIS JOHN L
E38 1 AU=FRANCIS JONATHAN M
E39 3 AU=FRANCIS JONATHAN W
E40 10 AU=FRANCIS JOSEPH
E41 1 AU=FRANCIS JOSEPH P
E42 2 AU=FRANCIS JOSEPH T
E43 1 AU=FRANCIS JOSHUA
E44 1 AU=FRANCIS JUDITH
E45 3 AU=FRANCIS JULIUS
E46 63 AU=FRANCIS K
E47 1 AU=FRANCIS K A
E48 10 AU=FRANCIS K C

S22 221 E3,E23-E26, E28, E31-E32, E40, E43-E45
S23 4 S19 AND S22

3/6/1 15802233 PMID: 12854151
Inhibition of HBV targeted ribonuclease enhanced by introduction of linker. Jul 2003

3/6/2 15377227 22613949 PMID: 12727273
Expression, purification, and efficacy of the type A botulinum neurotoxin catalytic domain fused to two translocation domain variants. May 2003

3/6/3 15317414 22773060 PMID: 12890769
Reversible suppression of glutamatergic neurotransmission of cerebellar granule cells in vivo by genetically manipulated expression of tetanus neurotoxin light chain. Jul 30 2003

3/6/4 15077658 22672520 PMID: 12787071
Two serine residues distinctly regulate the rescue function of Humanin, an inhibiting factor of Alzheimer's disease-related neurotoxicity : functional potentiation by isomerization and dimerization. Jun 2003

3/6/5 14856159 22420361 PMID: 12532452
Targeted ribonuclease can inhibit replication of hepatitis B virus. Feb 2003

3/6/6 14819242 22509330 PMID: 12622404
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Tissue inhibitor of metalloproteinase 1 inhibits excitotoxic cell death in neurons. Jan 2003

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Expression of a functional recombinant Phoneutria nigriventer toxin active on K+ channels. Mar 1 2003

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Smad3-dependent induction of plasminogen activator inhibitor-1 in astrocytes mediates neuroprotective activity of transforming growth factor-beta 1 against NMDA-induced necrosis. Dec 2002

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Plasma membrane targeting of SNAP-25 increases its local concentration and is necessary for SNARE complex formation and regulated exocytosis. Aug 15 2002

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Activation of GABA(A) receptors by guanidinoacetate: a novel pathophysiological mechanism. Nov 2002

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Production of an immunoenzymatic tracer combining a scFv and the acetylcholinesterase of Bungarus fasciatus by genetic recombination Jul 16 1999

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Enhancement of the endopeptidase activity of botulinum neurotoxin by its associated proteins and dithiothreitol. May 25 1999

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Neurexins are functional alpha-latrotoxin receptors. Mar 1999

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Recombinant and truncated tetanus neurotoxin light chain: cloning, expression, purification, and proteolytic activity. Mar 1999

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Conjugative transfer of the Escherichia coli-Clostridium perfringens shuttle vector pJIR1457 to Clostridium botulinum type A strains. Nov 1998

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Production of an expression system for a synaptobrevin fragment to monitor cleavage by botulinum neurotoxin B. Jul 1998

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Ganglioside GT1b as a complementary receptor component for Clostridium botulinum neurotoxins . Aug 1998

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Functional characterization of mongoose nicotinic acetylcholine receptor alpha-subunit: resistance to alpha-bungarotoxin and high sensitivity to acetylcholine. Jul 24 1998

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Transient expression of botulinum neurotoxin C1 light chain differentially inhibits calcium and glucose induced insulin secretion in clonal beta-cells. Dec 8 1997

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A new potassium channel toxin from the sea anemone Heteractis magnifica: isolation, cDNA cloning, and functional expression. Sep 23 1997

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Human immunodeficiency virus type 1 Tat protein induces death by apoptosis in primary human neuron cultures. Apr 1997

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A strongly interacting pair of residues on the contact surface of charybdotoxin and a Shaker K+ channel. Jan 1996

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Expression of a large, nontoxic fragment of botulinum neurotoxin serotype A and its use as an immunogen. Oct 1995

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Expression in Escherichia coli and purification of human eosinophil-derived neurotoxin with ribonuclease activity. Oct 1995

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17-beta estradiol protects neurons from oxidative stress-induced cell death in vitro. Nov 13 1995

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High affinity binding of alpha-latrotoxin to recombinant neurexin I alpha. Oct 13 1995

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Characterization of scorpion alpha-like toxin group using two new toxins from the scorpion Leiurus quinquestriatus hebraeus. Aug 2002

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Cytotoxic potency of cardiotoxin from Naja sputatrix: development of a new cytolytic assay. Aug 15 2002

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Refolding of the Escherichia coli expressed extracellular domain of alpha 7 nicotinic acetylcholine receptor. Jun 2002

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Caspase-3-dependent proteolytic cleavage of protein kinase Cdelta is essential for oxidative stress-mediated dopaminergic cell death a

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A unique approach for high level expression and production of a recombinant cobra neurotoxin in Escherichia coli. Apr 11 2002

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A rec ombinant scFv/streptavidin-binding peptide fusion protein for the quantitative determination of the scorpion venom neurotoxin Aahl. Nov 2001

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Biologically active sequence (KDI) mediates the neurite outgrowth function of the gamma-1 chain of laminin-1. Dec 15 2001

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Use o f fusion protein constructs to generate potent immunotherapy andprotection against scorpion toxins. Dec 12 2001

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Cytochrome c oxidase subunit Vb interacts with human androgen receptor: a potential mechanism for neurotoxicity in spinobulbar muscular atrophy. Oct-Nov 1 2001

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The neuronal calcium sensor protein VILIP-1 is associated with amyloid plaques and extracellular tangles in Alzheimer's disease and promotes cell death and tau phosphorylation in vitro: a link between calcium sensors and Alzheimer's disease? Oct 2001

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Neurotrophins prevent HIV Tat-induced neuronal apoptosis via a nuclear factor-kappaB (NF-kappaB)-dependent mechanism. Aug 2001

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A stoichiometric complex of neurexins and dystroglycan in brain. Jul 23 2001

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Role of alpha2-macroglobulin in regulating amyloid beta-protein neurotoxicity : protective or detrimental factor? Jul 2001

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A common exocytotic mechanism mediates axonal and dendritic outgrowth. Jun 1 2001

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Inhibition of neuronal nitric oxide synthase by N-phenacyl imidazoles. Feb 2001

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Membrane localization and biological activity of SNAP-25 cysteine mutants in insulin-secreting cells. Sep 2000

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Intratumoral administration of recombinant circularly permuted interleukin-4-Pseudomonas exotoxin in patients with high-grade glioma. Jun 2000

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Measurement of exocytosis by amperometry in adrenal chromaffin cells: effects of clostridial neurotoxins and activation of protein kinase C fusion pore kinetics. May 2000

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Cloning, expression, and one-step purification of the minimal essential domain of the light chain of botulinum neurotoxin type A. Jun 2000

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Functional characterization and mechanism of action of recombinant human kynurenine 3-hydroxylase. Feb 2000

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Microglial tissue plasminogen activator (tPA) triggers neuronal apoptosis in vitro. Feb 15 2000

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Recombinant adeno-associated viral vector-mediated glial cell line-derived neurotrophic factor gene transfer protects nigral dopamine neurons after onset of progressive degeneration in a rat model of Parkinson's disease. Nov 1999

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An in vivo assay for the identification of target proteases which cleave membrane-associated substrates. Dec 17 1999

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Expression and purification of the BmK M1 neurotoxin from the scorpion Buthus martensii Karsch. Dec 1999

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Cocaine reward and MPTP toxicity: alteration by regional variant dopamine transporter overexpression. Nov 10 1999

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Botulinum neurotoxin E-insensitive mutants of SNAP-25 fail to bind VAMP but support exocytosis. Dec 1999

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Neurotrophin-4/5 enhances survival of cultured spiral ganglion neurons and protects them from cisplatin neurotoxicity . Jul 1995

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Kainic acid-induced neuronal death is associated with DNA damage and a unique immediate-early gene response in c-fos-lacZ transgenic ra Jun 1995

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A mutated acetylcholine receptor subunit causes neuronal degeneration in C. elegans. Apr 1995

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Engineering of protein epitopes: a single deletion in a snake toxin generates full binding capacity to a previously unrecognized antibody. Jul 1

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Structural determinants of the blockade of N-type calcium channels by a peptide neurotoxin . Nov 17 1994

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Expression and characterization of recombinant human eosinophil-derived neurotoxin and eosinophil-derived neurotoxin -anti-transferrin receptor sFv. Oct 28 1994

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Competitive antagonism by phenylglycine derivatives at type I metabotropic glutamate receptors. Jun 1994

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Production of active, insect-specific scorpion neurotoxin in yeast. Jul 15 1994

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Functional expression and site-directed mutagenesis of a synthetic gene for alpha-bungarotoxin. Apr 15 1994

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Potentiation of N-methyl-D-aspartate-mediated brain injury by a human immunodeficiency virus-1-derived peptide in perinatal rodents. Aug 1993

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Effects of mutations of Torpedo acetylcholine receptor alpha 1 subunit residues 184-200 on alpha-bungarotoxin binding in a recombinant fusion protein. Sep 21 1993

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Characterization of a distinct binding site for the prokaryotic chaperone, GroEL, on a human granulocyte ribonuclease. Feb 25 1993

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Deposition of beta/A4 immunoreactivity and neuronal pathology in transgenic mice expressing the carboxyl-terminal fragment of the Alzheimer amyloid precursor in the brain. Nov 15 1992

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Insertion of a disulfide-containing neurotoxin into E. coli alkaline phosphatase: the hybrid retains both biological activities. Apr 1992

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Molecular neurotoxicology of trimethyltin: identification of stannin, a novel protein expressed in trimethyltin-sensitive cells. Jul 1992

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Cloning of a Clostridium botulinum type B toxin gene fragment encoding the N-terminus of the heavy chain. Feb 1 1992

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Substitution of Torpedo acetylcholine receptor alpha 1-subunit residues with snake alpha 1- and rat nerve alpha 3-subunit residues in recombinant fusion proteins: effect on alpha-bungarotoxin binding. Feb 11 1992

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Intracerebral implantation of nerve growth factor-producing fibroblasts protects striatum against neurotoxic levels of excitatory amino acids. 1991

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Calcium channel antagonists and human immunodeficiency virus coat protein-mediated neuronal injury. Jul 1991

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Characterization of the C3 gene of Clostridium botulinum types C and D and its expression in Escherichia coli. Oct 1991

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Expression and secretion of a functional scorpion insecticidal toxin in cultured mouse cells. Apr 1990

3/6/124 06680484 90306371 PMID: 2365072
A recombinant snake neurotoxin generated by chemical cleavage of a hybrid protein recovers full biological properties. Jun 18 1990

3/6/125 06458371 90083145 PMID: 2687847
Direct expression in E. coli of a functionally active protein A—snake toxin fusion protein. Nov 1989

3/6/126 06343017 89359352 PMID: 2670934
Cloning and expression of a synthetic gene for Cerebratulus lacteus neurotoxin B-IV. Sep 15 1989

3/7/26 DIALOG(R)File 155:MEDLINE(R) (c) format only 2004 The Dialog Corp. All rts. reserv.
11496293 98380521 PMID: 9712688
Ganglioside GT1b as a complementary receptor component for Clostridium botulinum neurotoxins .
Kozaki S; Kamata Y; Watarai S; Nishiki T; Mochida S
Department of Veterinary Science, College of Agriculture, Osaka Prefecture University, Sakai, Osaka, 599-8531, USA.
Microbial pathogenesis (ENGLAND) Aug 1998, 25 (2) p91-9, ISSN 0882-4010 Journal Code: 8606191
Document type: Journal Article Languages: ENGLISH Main Citation Owner: NLM Record type: Completed
Clostridium botulinum type B neurotoxin (BoNT/B) recognizesa complex of synaptotagmin II and ganglioside GT1b or GD1a a the high-affinity toxin binding site. Recombinant deletion mutants of synaptotagmin II allowed us to demonstrate that the N-terminal domain including the transmembrane region retains BoNT/B binding activity while the C-terminal domain is not involv in constituting the BoNT/B receptor. BoNT/B binding to reconstituted lipid vesicles containing synaptotagmin II and ganglioside showed that GT1b and GD1a confer the difference in the maximum binding capacity but not in the dissociation constant. The direct binding of GT1b to the deletion mutants revealed that the transmembrane region is required to bind GT1b, suggesting th synaptotagmin II binds to the ceramide portion of gangliosides within the plasma membrane. A monoclonal antibody against GT1b effectively inhibited not only BoNT/B binding to the reconstituted lipid vesicles and brain synaptosomes but also type A BoNT (BoNT/A) binding to brain synaptosomes. In addition, the monoclonal antibody antagonized the action of both BoNT/A a BoNT/B on synaptic transmission of rat superior cervical ganglion neurons. These results suggest that GT1b functions as a component of the receptor complex.Copyright 1998 Academic Press Record Date Created: 19980929 Record Date Complete 19980929

3/7/61 DIALOG(R)File 155:MEDLINE(R) (c) format only 2004 The Dialog Corp. All rts. reserv.
09938303 21850743 PMID: 11861082
A unique approach for high level expression and production of a recombinant cobra neurotoxin in Escherichia coli.
Wang Yongbao; Jing Liu; Xu Kangsen
School of Life Science, University of Science and Technology of China, Hefei, Anhui province, People's Republic of China. ybwang@nicpbp.org.cn
Journal of biotechnology (Netherlands) Apr 11 2002, 94 (3) p235-44, ISSN 0168-1656 Journal Code: 8411927
Document type: Journal Article Languages: ENGLISH Main Citation Owner: NLM Record type: Completed
In this report, we describe a simple approach to produce a large quantity of a recombinant cobra neurotoxin containing four p of disulfide bonds. A cDNA encoding the toxin was fused, in frame, to the carboxyl termini of thioredoxin via a linker sequence encoding two amino acids, Asp and Pro. Due to the presence of thioredoxin, a soluble form of the fusion protein was expresse in a compartment, sensitive to osmotic pressure, in Escherichia coli. The fusion protein was released into the solution with low ionic strength under an osmotic shock treatment, and purified in a single step using an ion exchange chromatography column. The purified protein was treated in diluted hydrochloric acid to induce hydrolysis of the protein at the Asp-Pro linker site. Then, the recombinant neurotoxin was purified by gel filtration of the acid-treated sample. When the biological activity of the purified toxin was assayed, it was as potent as the natural toxin. Using this protocol, approximately 12 mg of pure recombinant neurotoxin can be produced from one liter of bacterial culture. More importantly, this protocol can be easily used for the production of the toxin at a larger scale with low cost. The approach outlined in this report will be suitable for the production of other recombinant proteins especially those of the 'three-finger' family. Record Date Created: 20020225 Record Date Complet 20020517

3/7/117 DIALOG(R)File 155:MEDLINE(R) (c) format only 2004 The Dialog Corp. All rts. reserv.
07386559 92249751 PMID: 1577256
Cloning of a Clostridium botulinum type B toxin gene fragment encoding the N-terminus of the heavy chain.
Jung H H; Rhee S D; Yang K H
Department of Life Science, Korea Advanced Institute of Science and Technology, Taejon, Korea.
FEMS microbiology letters (NETHERLANDS) Feb 1 1992, 70 (1) p69-72, ISSN 0378-1097 Journal Code: 7705721
Document type: Journal Article Languages: ENGLISH Main Citation Owner: NLM Record type: Completed
Two lambda gt11 clones of the toxin gene of Clostridium botulinum type B were identified by the monoclonal antibody specific the heavy chain of type B toxin. Neither of the expressed fusion proteins from the lysates of lysogenic E. coli Y1089 showed a botulinal toxic activity. One of the clones hybridized to the oligonucleotide probe which was synthesized according to the amin acid sequence of N-terminus of heavy chain. The sequence analysis revealed that highly homologous regions in N-terminus o heavy chain exist among botulinum neurotoxins (type A, B) and tetanus toxin on the amino acid sequence level. Record Date Created: 19920611 Record Date Completed: 19920611

3/7/124 DIALOG(R)File 155:MEDLINE(R) (c) format only 2004 The Dialog Corp. All rts. reserv.
06680484 90306371 PMID: 2365072
A recombinant snake neurotoxin generated by chemical cleavage of a hybrid protein recovers full biological properties.

Boyot P; Pillet L; Ducancel F; Boulain J C; Tremeau O; Menez A
Departement de Biologie, Laboratoire d'Ingenierie des Proteines, C.E.N., Gif-sur-Yvette, France.
FEBS letters (NETHERLANDS) Jun 18 1990, 266 (1-2) p87-90, ISSN 0014-5793 Journal Code: 0155157
Erratum in FEBS Lett 1990 Oct 1;271(1-2) 258 Document type: Journal Article Languages: ENGLISH
Main Citation Owner: NLM Record type: Completed
We previously reported the production of a fused snake neurotoxin composed of protein A and erabutoxin a in E. coli. The hybrid had much lower toxicity and affinity for the acetylcholine nicotinic receptor than natural erabutoxin. By treating the hybrid with cyanogen bromide we generated a toxin which was purified in a single step by RP-HPLC. This compound, produced in a good yield, recovered all properties of native erabutoxin a, implying that the lower toxic activities of the hybrid were due to the bulky protein A and not to an incorrect folding of the toxin. This work serves as a basis for future studies of toxin-receptor interactions using engineered toxin mutants. Record Date Created: 19900814 Record Date Completed: 19900814

3/5/2 DIALOG(R)File 155:MEDLINE(R) (c) format only 2004 The Dialog Corp. All rts. reserv.
15377227 22613949 PMID: 12727273
Expression, purification, and efficacy of the type A botulinum neurotoxin catalytic domain fused to two translocation domain variants.
Jensen M J; Smith T J; Ahmed S A; Smith L A
Division of Toxinology and Aerobiology, United States Army Medical Research Institute of Infectious Diseases, 1425 Porter Street, Fort Detrick, MD 21702-5011, USA.
Toxicon - official journal of the International Society on Toxinology (England) May 2003, 41 (6) p691-701, ISSN 0041-0101 Journal Code: 1307333 Document type: Journal Article Languages: ENGLISH Main Citation Owner: NLM
Record type: Completed Subfile: INDEX MEDICUS
Clostridial neurotoxins are potent inhibitors of synaptic function, with the zinc-dependent proteolytic light chain (LC) portion of the toxin cleaving one of three neural SNARE proteins. In nature, the LC is expressed as a part of a much larger toxin and hemagglutinin complex, protecting it from environmental degradation and preserving its catalytic activity. We developed forms of the LC of type A botulinum neurotoxin (BoNT-A) with parts of the larger toxin gene, for use as reagents in high-throughput assays to screen for potential LC antagonists, to further elucidate the toxin's mechanism of action, and to study immunological responses to the toxin. Three BoNT-A constructs were engineered and expressed: the LC, LC with translocation region (LC+H(n)), and the LC with the belt portion of the translocation region (LC+Belt). Purification was optimized to a two-step process, with relatively high yields of all three constructs obtained. Activity assays showed all three constructs to be active, with the LC being the most active. Immunogenic protection against native BoNT-A toxin challenge was observed for all three constructs, with the best protection observed with the LC+H(n) and LC+Belt proteins.
Tags: Animal Descriptors: *Botulinum Toxin Type A--isolation and purification--IP; *Botulinum Toxin Type A--metabolism--ME; *Catalytic Domain; *Gene Expression; *Genetic Engineering; Botulinum Toxin Type A--genetics--GE; Botulinum Toxin Type A--immunology--IM; Enzyme-Linked Immunosorbent Assay; Mice; Protein Transport; Recombinant Fusion Proteins --chemistry--CH; Recombinant Fusion Proteins --immunology--IM; Recombinant Fusion Proteins --isolation and purification--IP; Recombinant Fusion Proteins --metabolism--ME; Temperature CAS Registry No.: 0 (Botulinum Toxin Type A); 0 (Recombinant Fusion Proteins)
Record Date Created: 20030502 Record Date Completed: 20030917

3/5/10 DIALOG(R)File 155:MEDLINE(R) (c) format only 2004 The Dialog Corp. All rts. reserv.
14546728 22135753 PMID: 12140265
Plasma membrane targeting of SNAP-25 increases its local concentration and is necessary for SNARE complex formation and regulated exocytosis.
Koticha Darshan K; McCarthy Ellen E; Baldini Giulia
Department of Anatomy and Cell Biology, Columbia University, College of Physicians and Surgeons, New York, NY 10032, USA.
Journal of cell science (England) Aug 15 2002, 115 (Pt 16) p3341-51, ISSN 0021-9533 Journal Code: 0052457
Contract/Grant No.: R01-DK53293; DK; NIDDK Document type: Journal Article Languages: ENGLISH
Main Citation Owner: NLM Record type: Completed Subfile: INDEX MEDICUS
SNAP-25 is an integral protein of the plasma membrane involved in neurotransmission and hormone secretion. The cysteine-rich domain of SNAP-25 is essential for membrane binding and plasma-membrane targeting. However, this domain is not required for SNARE complex formation and fusion of membranes in vitro. In this paper, we describe an 'intact-cell'-based system designed to compare the effect of similar amounts of membrane-bound and soluble SNAP-25 proteins on regulated exocytosis. In transfected neuroblastoma cells, Botulinum neurotoxin E (BoNT/E), a protease that cleaves SNAP-25, blocks regulated release of hormone. However, hormone release is rescued by expressing a wild-type SNAP-25 protein resistant to the toxin. BoNT/E-resistant SNAP-25 proteins lacking the cysteine-rich domain or with all the cysteines substituted by alanines do not form SNARE complexes or rescue regulated exocytosis when expressed at the same level as membrane-bound SNAP-25, which is approximately four-fold higher than the endogenous protein. We conclude that the cysteine-rich domain of SNAP-25 is essential for Ca(2+)-dependent hormone release because, by targeting SNAP-25 to the plasma membrane, it increases its local concentration, leading to the formation of enough SNARE complexes to support exocytosis.
Tags: Animal; Support, U.S. Gov't, P.H.S. Descriptors: *Cell Membrane--metabolism--ME; *Exocytosis--physiology--PH; *Membrane Proteins--metabolism--ME; *Nerve Tissue Proteins--metabolism--ME; *Protein Transport--physiology--PH; Amino Acid Sequence; Antigens, Surface --metabolism--ME; Botulinum Toxins--metabolism--ME; Calcium--metabolism--ME ; Cysteine--metabolism--ME; Genes, Reporter; Membrane Proteins--genetics --GE; Mice; Molecular Sequence Data; Nerve Tissue Proteins--genetics--GE; Pro-Opiomelanocortin--genetics--GE; Pro-Opiomelanocortin--metabolism--ME; Protein Conformation; Protein Structure, Tertiary; Recombinant Fusion Proteins --genetics--GE; Recombinant Fusion Proteins --metabolism--ME; Tumor Cells, Cultured CAS Registry No.: 0 (Antigens, Surface); 0 (Botulinum Toxins); 0 (Membrane Proteins); 0 (Nerve Tissue Proteins); 0 (Recombinant Fusion Proteins); 0 (SNAP receptor); 0 (botulinum toxin type E); 0 (synaptosomal-associated protein 25); 0 (syntaxin 1); 0 (vesicle-associated membrane protein); 52-90-4 (Cysteine); 66796-54-1 (Pro-Opiomelanocortin); 7440-70-2 (Calcium)
Record Date Created: 20020725 Record Date Completed: 20030311

3/5/17 DIALOG(R)File 155:MEDLINE(R) (c) format only 2004 The Dialog Corp. All rts. reserv.
11874546 99316188 PMID: 10387025
The functional role of positively charged amino acid side chains in alpha-bungarotoxin revealed by site-directed mutagenesis of a His-tagged recombinant alpha-bungarotoxin.
Rosenthal J A; Levandoski M M; Chang B; Potts J F; Shi Q L; Hawrot E
Department of Molecular Pharmacology, Physiology, and Biotechnology, Division of Biology and Medicine, Brown University, Providence, Rhode Island 02912, USA.
Biochemistry (UNITED STATES) Jun 15 1999, 38 (24) p7847-55, ISSN 0006-2960 Journal Code: 0370623
Contract/Grant No.: GM07601; GM; NIGMS; GM32629; GM; NIGMS; NS34348; NS; NINDS Document type: Journal Article
Languages: ENGLISH Main Citation Owner: NLM Record type: Completed Subfile: INDEX MEDICUS
A polyhistidine tag was added to the N-terminus of alpha-bungarotoxin (Bgtx) recombinantly expressed in E. coli. The His-tagged Bgtx was identical to native, venom-derived Bgtx in its apparent affinity for the nicotinic acetylcholine receptor (nAChR Torpedo electric organ membranes. Furthermore, in a physiological assay involving mouse muscle nAChR expressed in Xenopus oocytes, the His-tagged Bgtx was as effective as authentic Bgtx at blocking acetylcholine-evoked currents. Ala-substitution mutagenesis of His-tagged Bgtx was used to evaluate the functional contribution of Arg36, a residue that is invaria among all alpha- neurotoxins . Replacement with Ala resulted in a 90-fold decrease in the apparent affinity for the Torpedo nAChR and a corresponding 150-fold increase in the IC50 for block of heterologously expressed mouse muscle nAChR, demonstrating the critical importance of this positive charge for the binding and functional activity of a long alpha- neurotoxin . The observed decrease in affinity corresponds to a DeltaDeltaG of 2.7 kcal/mol and indicates that Arg36 makes a major contribution to complex formation. This finding is consistent with the proposal that Arg36 mimics the positive charge found on acetylcholine and directs the toxin to interact with receptor sites normally involved in acetylcholine recognition. In comparison, Ala-substitution of the highly conserved Lys26 resulted in only a 9-fold decrease in apparent affinity. Truncation of the His-tagg Bgtx following residue 67 produces a toxin lacking the seven C-terminal residues including the two positively charged residues Lys70 and Arg72. Truncation leads to a 7-fold decrease in apparent binding affinity.
Tags: Animal; Support, U.S. Gov't, P.H.S. Descriptors: Amino Acids--physiology--PH; *Bungarotoxins--physiology--PH; *Histidine--genetics--G *Mutagenesis, Site-Directed; * Recombinant Fusion Proteins --metabolism--ME; Amino Acid Substitution--genetics--GE; Amino Acids--genetic GE; Amino Acids--metabolism--ME; Bacteriophage T4 --genetics--GE; Binding, Competitive--genetics--GE; Bungarotoxins--genetics --GE; Bungarotoxins--metabolism--ME; Escherichia coli--genetics--GE; Genetic Vectors--metabolism--ME; Genetic Vectors--pharmacology--PD; Histidine--metabolism--ME; Hydrogen-Ion Concentration; Mice; Muscle, Skeletal--drug effects--DE; Muscle, Skeletal--metabolism--ME; Nicotinic Antagonists--pharmacology--PD; Receptors, Nicotinic--biosynthesis--BI; Recombinant Fusion Proteins --isolation and purification-Recombinant Fusion Proteins --pharmacology--PD; Sequence Deletion; Torpedo ; Viral Proteins--genetics--GE CAS Registry No.: 0 (Amino Acids); 0 (Bungarotoxins); 0 (Genetic Vectors); 0 (Nicotinic Antagonists); 0 (Receptors, Nicotinic); 0 (Recombinant Fusion Proteins); 0 (Viral Proteins); 147258-48-8 (bacteriophage T4 gene 9 protein); 71-00-1 (Histidine)
Record Date Created: 19990715 Record Date Completed: 19990715

3/5/21 DIALOG(R)File 155:MEDLINE(R) (c) format only 2004 The Dialog Corp. All rts. reserv.
11723801 99160489 PMID: 10049679
Recombinant and truncated tetanus neurotoxin light chain: cloning, expression, purification, and proteolytic activity.
Tonello F; Pellizzari R; Pasqualato S; Grandi G; Peggion E; Montecucco C
Dipartimento di Scienze Biomediche, Universita di Padova, Padova I-35121, Italy.
Protein expression and purification (UNITED STATES) Mar 1999, 15 (2) p221-7, ISSN 1046-5928 Journal Code: 910149
Document type: Journal Article Languages: ENGLISH Main Citation Owner: NLM Record type: Completed
Subfile: INDEX MEDICUS
Tetanus neurotoxin (TeNT) consists of two disulfide-linked polypeptide chains, heavy (H) and light (L). The L chain is a zinc endopeptidase protein highly specific for vesicle-associated membrane protein (VAMP), which is an essential component of th exocytosis apparatus. Here we describe the cloning of the L chain of TeNT from Clostridium tetani strain Y-IV-3 (WS 15) and i expression in Escherichia coli as a glutathione S-transferase fusion protein. The full-length recombinant L chain, correspondin to residues 1-457, was obtained as a mixture of proteins of slightly different mass with identical N-terminal ends. To obtain a product useful for structural analysis and crystallization, a COOH-terminally truncated L chain (residues 1-427) was cloned, expressed, and purified with high yield. This truncated L chain is more active than the full-length and wild-type proteins in the hydrolysis of VAMP. Preliminary experiments of crystallization of the truncated recombinant L chain gave encouraging results. Copyright 1999 Academic Press.
Tags: Human; Support, Non-U.S. Gov't Descriptors: *Metalloendopeptidases--genetics--GE; *Tetanus Toxin --genetics--GE; Cloning, Molecular; Crystallization; Escherichia coli; Gene Expression; Membrane Proteins--metabolism--ME; Metalloendopeptidases --biosynthesis--B Metalloendopeptidases--isolation and purification--IP; Metalloendopeptidases--metabolism--ME; Peptide Fragments--biosynthesis--BI ; Peptide Fragments--genetics--GE; Peptide Fragments --isolation and purification--IP; Peptide Fragments--metabolism--ME; Recombinant Fusion Proteins --biosynthesis-- I; Recombinant Fusion Proteins --genetics--GE; Recombinant Fusion Proteins --isolation and purification--IP;

Recombinant Fusion Proteins --metabolism--ME; Spectrometry, Fluorescence; Substrate Specificity; Tetanus Toxin--biosynthesis--BI; Tetanus Toxin --isolation and purification--IP; Tetanus Toxin--metabolism--ME CAS Registry No.: 0 (Membrane Proteins); 0 (Peptide Fragments); 0 (Recombinant Fusion Proteins); 0 (Tetanus Toxin); 0 (vesicle-associated membrane protein) Enzyme No.: EC 3.4.24 (Metalloendopeptidases); EC 3.4.24.- (zinc-endopeptidase, tetanus neurotoxin)
Record Date Created: 19990511 Record Date Completed: 19990511

7/6/1 14867997 22451921 PMID: 12563791
[Association expression of genes encoding gst of Schistosoma japonicum and enterotoxigenic Escherichia coli] 1999

7/6/2 12007058 99452975 PMID: 10521470
Involvement of small GTPases in Mycoplasma fermentans membrane lipoproteins-mediated activation of macrophages. Oct 22 1999

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The transcriptional activator CorR is involved in biosynthesis of the phytotoxin coronatine and binds to the cmaABT promoter region in a temperature-dependent manner. Sep 1999

7/6/4 11976922 99421861 PMID: 10491008
IL-2 receptor-targeted cytolytic IL-2/Fc fusion protein treatment blocks diabetogenic autoimmunity in nonobese diabetic mice. Oct 1 1999

7/6/5 11974124 99419014 PMID: 10488072
Neosynthesis and activation of Rho by Escherichia coli cytotoxic necrotizing factor (CNF1) reverse cytopathic effects of ADP-ribosylated Rho. Sep 24 1999

7/6/6 11954727 99399090 PMID: 10470104
Wortmannin, a phosphoinositide 3-kinase inhibitor, selectively enhances cytotoxicity of receptor-directed-toxin chimeras in vitro and in vivo. May-Jun 1999

7/6/7 11942739 99386678 PMID: 10455034
Analysis of agonist function at fusion proteins between the IP prostanoid receptor and cognate, unnatural and chimaeric G-proteins. Sep 1 1999

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The Xanthomonas Hrp type III system secretes proteins from plant and mammalian bacterial pathogens. Aug 3 1999

7/6/9 11914297 99357644 PMID: 10427035
Activation process of cipteran-specific insecticidal protein produced by Bacillus thuringiensis subsp. israelensis. Aug 1999

7/6/10 11905255 99348356 PMID: 10419539
Yersinia enterocolitica type III secretion. On the role of SycE in targeting YopE into HeLa cells. Jul 30 1999

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Ion channel activity of the BH3 only Bcl-2 family member, BID. Jul 30 1999

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The 5' region of cnf1 harbours a translational regulatory mechanism for CNF1 synthesis and encodes the cell-binding domain of the toxin. Jul 1999

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Exploiting retrograde transport of Shiga-like toxin 1 for the delivery of exogenous antigens into the MHC class I presentation pathway. Jun 18 1999

7/6/14 11882109 99323920 PMID: 10393809
Rvs167p, the budding yeast homolog of amphiphysin, colocalizes with actin patches. Aug 1999

7/6/15 11865823 99307182 PMID: 10377103
Cytotoxic T-lymphocyte epitopes fused to anthrax toxin induce protective antiviral immunity. Jul 1999

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An anti-CD30 single-chain Fv selected by phage display and fused to Pseudomonas exotoxin A (Ki-4(scFv)-ETA') is a potent immunotoxin against a Hodgkin-derived cell line. Jun 1999

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Development of a recombinant interleukin-4-Pseudomonas exotoxin for therapy of glioblastoma. Jan-Feb 1999

7/6/18 11847433 99288230 PMID: 10336877
High-level expression and purification of the recombinant diphtheria fusion toxin DTGM for PHASE I clinical trials. Jun 1999

7/6/19 11815887 99255537 PMID: 10322014
Direct interaction of the EpsL and EpsM proteins of the general secretion apparatus in Vibrio cholerae. May 1999

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Cloning and cytotoxicity of fusion proteins of EGF and angiogenin. 1999

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Intranuclear delivery of an antiviral peptide mediated by the B subunit of Escherichia coli heat-labile enterotoxin. Apr 27 1999

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Crystallization and preliminary X-ray diffraction studies of the 51 kDa protein of the mosquito-larvicidal binary toxin from Bacillus sphaericus. Ma 1999

7/6/23 11775824 99214180 PMID: 10196187
A novel cytotoxin from Clostridium difficile serogroup F is a functional hybrid between two other large clostridial cytotoxins. Apr 16 1999

7/6/24 11771897 99210155 PMID: 10195780
Novel modifications to the C-terminus of LTB that facilitate site-directed chemical coupling of antigens and the development of LTB as a carrier for mucosal vaccines. Mar 17 1999

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A new series of pET-derived vectors for high efficiency expression of Pseudomonas exotoxin-based fusion proteins. Mar 18 1999

7/6/26 11755179 99192697 PMID: 10089527
Crystallization and preliminary X-ray diffraction studies of alpha-toxin from two different strains (NCTC8237 and CER89L43) of Clostridium perfringens. Nov 1 1998

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Intracellular targeting of the endoplasmic reticulum/nuclear envelope by retrograde transport may determine cell hypersensitivity to verotoxin globotriaosyl ceramide fatty acid isoform traffic. Dec 1998

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Solution structure of BID, an intracellular amplifier of apoptotic signaling. Mar 5 1999

7/6/29 11747698 99185011 PMID: 10085027
Oligomerization of anthrax toxin protective antigen and binding of lethal factor during endocytic uptake into mammalian cells. Apr 1999

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An Arcanobacterium (Actinomyces) pyogenes mutant deficient in production of the pore-forming cytolysin pyolysin has reduced virulence. Apr 1999

7/6/31 11720993 99157583 PMID: 10048023
Expression and properties of an aerolysin--Clostridium septicum alpha toxin hybrid protein. Feb 1999

7/6/32 11720819 99157408 PMID: 10047878
Differential activity of cholera toxin and E. coli enterotoxin: construction and purification of mutant and hybrid derivatives. Nov 1998

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The KDEL retrieval system is exploited by Pseudomonas exotoxin A, but not by Shiga-like toxin-1, during retrograde transport from the Golgi complex to the endoplasmic reticulum. Feb 1999

7/6/34 11680158 99115517 PMID: 9916051
Deam idation of Cdc42 and Rac by Escherichia coli cytotoxic necrotizing factor 1: activation of c-Jun N-terminal kinase in HeLa cells. Feb 19

7/6/35 11672041 99107223 PMID: 9892205
Vascular endothelial growth factor chimeric toxin is highly active against endothelial cells. Jan 1 1999

7/6/36 11657978 99092760 PMID: 9876933
Stepwise transplantation of an active site loop between heat-labile enterotoxins LT-II and LT-I and characterization of the obtained hybrid toxins . Nov 1998

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Gating of skeletal and cardiac muscle sodium channels in mammalian cells. Jan 15 1999

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Characterization of membrane translocation by anthrax protective antigen. Nov 10 1998

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Positive selection vectors to generate fused genes for the expression of his-tagged proteins. Nov 1998

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Functional interactions between chpB and parD, two homologous conditional killer systems found in the Escherichia coli chromosome and in plasmid R1. Nov 1 1998

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Prokaryotic expression of porcine epidemic diarrhoea virus ORF3. 1998

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Crystallization of ccdB. Sep 1 1998

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Bacterial phospholipases. 1998

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Differe nces in cytotoxicity of native and engineered RIPs can be used to assess their ability to reach the cytoplasm. Aug 28 1998

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Improved stability and yield of a Fv-toxin fusion protein by computer design and protein engineering of the Fv. Sep 4 1998

7/6/46 11502057 98386734 PMID: 9720265
Recombinant antibody fragments. Aug 1998

7/6/47 11496172 98380400 PMID: 9712803
Actino bacillus actinomycetemcomitans leukotoxin induces apoptosis in HL-60 cells. Sep 1998

7/6/48 11469699 98353391 PMID: 9687463
Phage display of a biologically active Bacillus thuringiensis toxin.Aug 1998

7/6/49 11435654 98318336 PMID: 9655604
Nicotinic agonists competitively antagonize serotonin at mouse 5-HT3 receptors expressed in Xenopus oocytes. May 15 1998

7/6/50 11430324 98312844 PMID: 9650824
Afferent signals to the CNS appear not to condition the modulation of interleukin-1 receptors in the hippocampus. Sep-Dec 1997

7/6/51 11412641 98294443 PMID: 9630987
An Escherichia coli hemolysin transport system-based vector for the export of polypeptides: export of Shiga-like toxin IIeB subunit by Salmonella typhimurium aroA. Jun 1996

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Recombinant immunotoxins and chimeric toxins for targeted therapy in oncology] Immunotoxines recombinantes et toxines chimeres pour une therapie ciblee en oncologie. Dec 1997

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Proteolytic inactivation of MAP-kinase-kinase by anthrax lethal factor. May 1 1998

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Recombinant heregulin-Pseudomonas exotoxin fusion proteins: interactions with the heregulin receptors and antitumor activity in vivo. Apr 1998

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Increasing immunogenicity of antigens fused to Ig-binding proteins by cell surface targeting. Apr 15 1998

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A modular DNA carrier protein based on the structure of diphtheria toxin mediates target cell-specific gene delivery. Apr 10 1998

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The biochemistry of hemolysin toxin activation: characterization of HlyC, an internal protein acyltransferase. Mar 31 1998

7/6/58 11308636 98187903 PMID: 9529054
The N-terminal part of the enzyme component (C2I) of the binary Clostridium botulinum C2 toxin interacts with the binding component 2II and functions as a carrier system for a Rho ADP-ribosylating C3-like fusion toxin. Apr 1998

7/6/59 11308445 98187712 PMID: 9528863
Betacellulin-Pseudomonas toxin fusion proteins bind but are not cytotoxic to cells expressing HER4; correlation of EGFR for cytotoxic activity. Mar 5 1998

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Involvement of glutamic acid residue at position 7 in the formation of the intramolecular disulfide bond of Escherichia coli heat-stable enterotoxin Ip in vivo. Mar 1998

7/6/61 11298186 98177234 PMID: 9508786
Internalization of a Bacillus anthracis protective antigen-c-Myc fusion protein mediated by cell surface anti-c-Myc antibodies. Feb 1998

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Chimeric clostridial cytotoxins: identification of the N-terminal region involved in protein substrate recognition. Mar 1998

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Site directed mutagenesis of histidine residues in anthrax toxin lethal factor binding domain reduces toxicity. Dec 1997

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Construction and characterization of versatile cloning vectors for efficient delivery of native foreign proteins to the periplasm of Escherichia coli. 1997

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Getting plant toxins to fuse. Oct 1997

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A recombinant GM-CSF-PE40 ligand toxin is functionally active but not cytotoxic to cells. Jun 1997

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Epitope conservation and immunohistochemical localization of the guanylin/stable toxin peptide receptor, guanylyl cyclase C. Sep 15 1997

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Characterization and receptor specific toxicity of two diphtheria toxin-related interleukin-3 fusion proteins DAB389-mIL-3 and DAB389-(Gly4Ser)2-mIL-3. Apr 7 1997

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In vitro effects of a recombinant toxin, mSCF-PE40, targeting c-kit receptors ectopically expressed in small cell lung cancers. Feb 26 1997

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A new class of antigen-specific killer cells. Jan 1997

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Homologues of the human multidrug resistance genes MRP and MDR contribute to heavy metal resistance in the soil nematode Caenorhabditis elegans. Nov 15 1996

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Interaction of Ca2(+)-activated K+ channels with refolded charybdotoxins mutated at a central interaction residue. 1996

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Molec ular and biochemical characterization of a heat-labile cytotonic enterotoxin from Aeromonas hydrophila. Nov 1996

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Use of Vibrio spp. for expression of Escherichia coli enterotoxin B subunit fusion proteins: purification and characterization of a chimera containing a C-terminal fragment of DNA polymerase from herpes simplex virus type 1. Nov 1996

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Potent antitumour activity of a new class of tumour-specific killer cells. Jan 2 1997

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Preclinical development of a recombinant toxin containing circularly permuted interleukin 4 and truncated Pseudomonas exotoxin for therapy of malignant astrocytoma. Dec 15 1996

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Characterization of a ricin fusion toxin targeted to the interleukin-2 receptor. Oct 1996

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A recombinant Escherichia coli heat-stable enterotoxin b (STb) fusion protein eliciting neutralizing antibodies. Apr 1996

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Fused polycationic peptide mediates delivery of diphtheria toxin A chain to the cytosol in the presence of anthrax protective antigen. Aug 6 19

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The pe rformance of e23(Fv)PEs, recombinant toxins targeting the erbB-2 protein. Apr 1996

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A recombinant insect-specific alpha-toxin of Buthus occitanus tunetanus scorpion confers protection against homologous mammal toxins . Jun 1996

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Amino acid residues in the pro region of Escherichia coli heat-stable enterotoxin I that affect efficiency of translocation across the inner membrane. Jul 1996

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A continuous epitope from transmissible gastroenteritis virus S protein fused to E. coli heat-labile toxin B subunit expressed by attenuated Salmonella induces serum and secretory immunity. Mar 1996

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An improved circularly permuted interleukin 4-toxin is highly cytotoxic to human renal cell carcinoma cells. Introduction of gamma c chain in RCC cells does not improve sensitivity. Jul 10 1996

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Single-chain fusion toxins for the treatment of breast cancer: antitumor activity of BR96 sFv-PE40 and heregulin-PE40. 1996

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New gene from nine Bacillus sphaericus strains encoding highly conserved 35.8-kilodalton mosquitocidal toxins . Jun 1996

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Translational fusion of heat labile enterotoxin chain B and beta-subunit of human chorionic gonadotropin: periplasmic expression in Escherichia coli and its immunogenicity. May 27 1996

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Target cell-specific DNA transfer mediated by a chimeric multidomain protein. Novel non-viral gene delivery system. May 3 1996

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Domain III substitution in Bacillus thuringiensis delta-endotoxin CryIA(b) results in superior toxicity for Spodoptera exigua and altered membrane protein recognition. May 1996

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Analysis of cryIAa expression in sigE and sigK mutants of Bacillus thuringiensis. Apr 10 1996

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Plasmid RK2 toxin protein ParE: purification and interaction with the ParD antitoxin protein. Mar 1996

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Cytotoxicity of KDEL-terminated ricin toxins correlates with distribution of the KDEL receptor in the Golgi. Feb 1996

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A specific targeting domain in mature exotoxin A is required for its extracellular secretion from Pseudomonas aeruginosa. Jan 15 1996

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IL2-ricin fusion toxin is selectively cytotoxic in vitro to IL2 receptor-bearing tumor cells. Nov-Dec 1995

7/6/140 10360272 96163481 PMID: 8575456
Lipid interaction of the 37-kDa and 58-kDa fragments of the Helicobacter pylori cytotoxin. Dec 15 1995

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Targeting diphtheria toxin to growth factor receptors. Oct 1995

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Improved expression of toxic proteins in E coli. Aug 1995

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Identification by in vitro complementation of regions required for cell-invasive activity of Bordetella pertussis adenylate cyclase toxin. Sep 1995

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Disruption of herpes simplex virus ribonucleotide reductase quaternary structure by peptide inhibitors as a novel approach to antiviral therapy. Oct 1995

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Characterization of an internal permissive site in the cholera toxin B-subunit and insertion of epitopes from human immunodeficiency virus-1, hepatitis B virus and enterotoxigenic Escherichia coli. Nov 20 1995

7/6/147 10285718 96087571 PMID: 8522489
Experimental therapies in the treatment of cutaneous T-cell lymphoma. Oct 1995

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A proposed mechanism of ADP-ribosylation catalyzed by the pertussis toxin S1 subunit. 1995

7/6/149 10240727 96042092 PMID: 7592381
A modified two-component regulatory system is involved in temperature-dependent biosynthesis of the Pseudomonas syringae phytotoxi coronatine. Nov 1995

7/6/150 10230919 96032221 PMID: 7549113
Identification of the essential regions for LukS- and H gamma II-specific functions of staphylococcal leukocidin and gamma-hemolysin. Aug 19

7/5/4 DIALOG(R)File 155:MEDLINE(R) (c) format only 2004 The Dialog Corp. All rts. reserv.
11976922 99421861 PMID: 10491008
IL-2 receptor-targeted cytolytic IL-2/Fc fusion protein treatment blocks diabetogenic autoimmunity in nonobese diabetic mice
Zheng X X; Steele A W; Hancock W W; Kawamoto K; Li X C; Nickerson P W; Li Y; Tian Y; Strom T B
Department of Medicine, Division of Immunology, Beth Israel Deaconess Medical Center, Harvard Medical School, Boston MA 02215, USA.
Journal of immunology (Baltimore, Md. - 1950) (UNITED STATES) Oct 1 1999 , 163 (7) p4041-8, ISSN 0022-1767 Journal Code: 2985117R Document type: Journal Article Languages: ENGLISH Main Citation Owner: NLM
Record type: Completed Subfile: AIM; INDEX MEDICUS; AIDS/HIV
High affinity IL-2R5 is present on recently activated but not on resting or memory T cells. Selective targeting of T cells bearing high affinity IL-2R is an attractive therapy for many T cell-dependent cytopathic disease processes. A variety of rodent mAbs directed against the alpha-chain of the IL-2R, as well as IL-2 fusion toxins , have been used in animals and humans to achieve selective immunosuppression. Here we report on the development of a novel IL-2R targeting agent, a cytolytic chimeric IL-2/F fusion protein. This immunoligand binds specifically and with high affinity to IL-2R and is structurally capable of recruiting host Ab-dependent cell-mediated cytotoxicity and complement-dependent cytotoxicity activities. The Ig component ensures an extended circulating t1/2 of 25 h following systemic administration. To subsequently explore the mechanisms of the antidiabetogenic effects of IL-2/Fc, we have mutated the FcR binding and complement C1q binding (Fc-/-) domains of the Fc fragment to render the Fc unable to direct Ab-dependent cell-mediated cytotoxicity and complement-dependent cytotoxicity activities. In a model of passive transfer of diabetes in nonobese diabetic mice, lytic IL-2/Fc, but not nonlytic IL-2/Fc-/-, exhibite striking antidiabetogenic effects. Together with the negligible potential of IL-2/Fc for immunogenicity, this finding forecasts that cytolytic IL-2/Fc may offer a new therapeutic approach for selective targeting of auto and alloimmune T cells.
Tags: Animal; Female; Male; Support, Non-U.S. Gov't; Support, U.S. Gov't, P.H.S. Descriptors: Cytotoxicity, Immunologic--genetics--GE; *Diabetes Mellitus, Insulin-Dependent--immunology--IM; *Diabetes Mellitus, Insulin-Dependent --prevention and control--PC; *Gene Therapy; *Immunoglobulins, Fc--genetics --GE; *Interleukin-2--genetics--GE; *Receptors, Interleukin-2--genetics--GE ; * Recombinant Fusion Proteins immunology--IM; Adoptive Transfer; Antibodies, Monoclonal--administration and dosage--AD; Antigens, CD4 --immunology--IM; Blotting, Western; CD4 Lymphocyte Count; Diabetes Mellitus, Insulin-Dependent--genetics--GE; Diabetes Mellitus, Insulin-Dependent--pathology--P Gene Targeting; Half-Life; Immunoglobulin s, Fc--therapeutic use--TU; Injections, Intraperitoneal; Interleukin-2 --therapeutic use--TU; Lymphocyte Depletion; Mice; Mice, Inbred BALB C; Mice, Inbred NOD; Recombinant Fusion Proteins --blood--BL; Recombinant Fusion Proteins --chemistry--CH; Recombinant Fusion Proteins --therapeutic use--TU CAS Registry No.: 0 (Antibodies, Monoclonal); 0 (Antigens CD4); 0 (Immunoglobulins, Fc); 0 (Interleukin-2); 0 (Receptors, Interleukin-2) ; 0 (Recombinant Fusion Proteins)
Record Date Created: 19991021 Record Date Completed: 19991021

7/5/13 DIALOG(R)File 155:MEDLINE(R) (c) format only 2004 The Dialog Corp. All rts. reserv.
11887991 99330177 PMID: 10403383
Exploiting retrograde transport of Shiga-like toxin 1 for the delivery of exogenous antigens into the MHC class I presentation pathway.
Noakes K L; Teisserenc H T; Lord J M; Dunbar P R; Cerundolo V; Roberts L M
Department of Biological Sciences, University of Warwick, Coventry, UK.
FEBS letters (NETHERLANDS) Jun 18 1999 , 453 (1-2) p95-9, ISSN 0014-5793 Journal Code: 0155157
Document type: Journal Article Languages: ENGLISH Main Citation Owner: NLM Record type: Completed
Subfile: INDEX MEDICUS
Shiga-like toxin 1 (SLT) from Escherichia coli O157:H7 enters mammalian cells by endocytosis from the cell surface to the endoplasmic reticulum before translocating into the cytosol. Here, SLT was engineered at its N- or C-terminus to carry a peptid derived from influenza virus Matrix protein for delivery to major histocompatibility complex (MHC) class I molecules. We show that SLT N-Ma was capable of sensitising cells for lysis by appropriate cytotoxic T-lymphocytes whilst no killing of SLT-resista cells was observed. Our results demonstrate that peptide was liberated intracellularly and that retrograde transport of a disarm cytotoxic protein can intersect the MHC class 1 presentation pathway.
Tags: Support, Non-U.S. Gov't Descriptors: Antigen Presentation; *Antigens, Viral--metabolism--ME; *Bacterial Toxins --immunology--IM; *Histocompatibility Antigens Class I; *Viral Matrix Proteins--immunology--IM; Antigens, Viral--genetics--GE Antigens, Viral--immunology--IM; Bacterial Toxins --genetics--GE; Bacterial Toxins --metabolism--ME; Biological Transpo Cytotoxicity, Immunologic; Endoplasmic Reticulum--metabolism--ME; Recombinant Fusion Proteins --immunology--IM; Recombinant Fusion Proteins --metabolism--ME; Shiga-Like Toxin I; T-Lymphocytes, Cytotoxic--immunology--IM; Viral Matrix Proteins--genetics--GE; Viral Matrix Proteins--metabolism--ME CAS Registry No.: 0 (Antigens, Viral); 0 (Bacterial Toxins (Histocompatibility Antigens Class I); 0 (Recombinant Fusion Proteins); 0 (Shiga-Like Toxin I); 0 (Viral Matrix Proteins); 0 (influenza virus membrane protein)
Record Date Created: 19990802 Record Date Completed: 19990802

7/5/17 DIALOG(R)File 155:MEDLINE(R) (c) format only 2004 The Dialog Corp. All rts. reserv.
11853088 99294094 PMID: 10367674
Development of a recombinant interleukin-4-Pseudomonas exotoxin for therapy of glioblastoma.
Puri R K
Laboratory of Molecular Tumor Biology, Division of Cellular and Gene Therapies, Center for Biologics Evaluation and Research, Food and Drug Administration, Bethesda, Maryland 20892, USA.
Toxicologic pathology (UNITED STATES) Jan-Feb 1999 , 27 (1) p53-7, ISSN 0192-6233 Journal Code: 7905907
Document type: Journal Article; Review; Review, Tutorial Languages: ENGLISH Main Citation Owner: NLM
Record type: Completed Subfile: INDEX MEDICUS
About 12,000 Americans are diagnosed with malignant astrocytoma each year. Despite surgery, radiotherapy, and chemotherapy, the prognosis of these patients remains poor. Targeted toxins based on the identification of novel antigens or receptors provide a promising new approach to treating cancer. We have identified one such cell surface protein in the form of interleukin (IL)-4 receptors (IL-4R) on human malignant astrocytoma. Normal brain tissues from frontal cortex and temporal lobe cortex do not express IL-4R. To target IL-4R, we generated a chimeric fusion protein composed of IL-4 and Pseudomonas exotoxin (IL4-PE). This toxin is highly cytotoxic to IL-4R-bearing human brain cancer cells. Preclinical toxicologic experiments were performed in mice, rats, and guinea pigs to determine an maximum tolerated dose. Intrathecal administration in cynomolgus monkeys produced high cerebrospinal fluid levels without any central nervous system or other abnormalities. When IL4-PE was injected into the right frontal cortex of rats, localized necrosis was observed at 1,000 but not < or =100 microg/ml doses. Intravenous administration of this biologic to monkeys produced reversible grade 3 or grade 4 elevations of hepatic enzymes in a dose-dependent manner. These results indicate that localized administration can produce nontoxic levels of IL4-PE that may have significant activity against astrocytoma. In vivo experiments with nude mice have demonstrated that IL4-PE has significant antitumor activity against human glioblastoma tumor model. Intratumor administration of IL4-PE has been initiated for the treatment of malignant astrocytoma in a phase I clinical trial. (28 Refs.)
Tags: Animal; Human Descriptors: *Brain Neoplasms--therapy--TH; *Exotoxins--pharmacology--PD; *Glioblastoma--therapy--TH; *Interleukin-4--pharmacology--PD; *Pseudomonas --genetics--GE; Bacterial Proteins--genetics--GE; Brain Neoplasms --metabolism--ME; Drug Design; Exotoxins--chemical synthesis--CS; Exotoxins--therapeutic use--TU; Glioblastoma--metabolism--ME; Interleukin- 4--chemical synthesis--CS; Interleukin-4--therapeutic use--TU; Recombinant Fusion Proteins --chemical synthesis--CS; Recombinant Fusion Proteins --pharmacology--PD; Recombinant Fusion Proteins --therapeutic use--TU CAS Registry No.: 0 (Bacterial Proteins); 0 (Exotoxins); 0 (IL-4-PE40 chimeric protein); 0 (Recombinant Fusion Proteins); 207137-56-2 (Interleukin-4) Enzyme No.: EC 2.4.2.31 (exotoxin A, Pseudomonas aeruginosa)
Record Date Created: 19990729 Record Date Completed: 19990729

7/5/18 DIALOG(R)File 155:MEDLINE(R) (c) format only 2004 The Dialog Corp. All rts. reserv.
11847433 99288230 PMID: 10336877
High-level expression and purification of the recombinant diphtheria fusion toxin DTGM for PHASE I clinical trials.
Frankel A E; Ramage J; Latimer A; Feely T; Delatte S; Hall P; Tagge E; Kreitman R; Willingham M
Department of Cancer Biology, Wake Forest University School of Medicine, Winston-Salem, North Carolina 27157, USA. afrankel@wfubmc.edu
Protein expression and purification (UNITED STATES) Jun 1999 , 16 (1) p190-201, ISSN 1046-5928 Journal Code: 9101496 Contract/Grant No.: NIHR0176738; HR; NHLBI Document type: Clinical Trial; Clinical Trial, Phase I; Journal Article
Languages: ENGLISH Main Citation Owner: NLM Record type: Completed Subfile: INDEX MEDICUS
A genetically engineered fusion toxin targeted to acute myeloid leukemic (AML) blasts was designed with the first 388 amino acid residues of diphtheria toxin with an H-M linker fused to human granulocyte-macrophage colony-stimulating factor. The cDNA was subcloned in the pRK bacterial expression plasmid and used to transform BL21 (DE3) Escherichia coli harboring pUBS500 plasmid. Transformants were grown in Superbroth and induced with IPTG. Inclusion bodies were isolated, washed, and denatured in guanidine hydrochloride with dithioerythritol. Recombinant protein was refolded by diluting 100-fold in cold buffer with arginine and oxidized glutathione. After dialysis, purified protein was obtained after anion-exchange, size exclusion on FPLC, and polymixin B affinity chromatography. The final material was filter sterilized, aseptically vialed, and stored at -80 degrees C. Fifty-four 3-liter bacterial culture preparations were made and pooled into 27 batches. The final product was characterized by Coomassie Plus protein assay, Coomassie-stained SDS-PAGE, limulus amebocyte lysate endotoxin assay, human AML HL60 cell cytotoxicity assay, HPLC TSK3000, N-terminal sequencing, E. coli DNA contamination, C57BL6 mouse toxicity, and immunohistochemistry. Yields were 23 mg/liter bacterial culture of denatured fusion toxin. After refolding and chromatography, final yields were 24 +/- 4% or 5 mg/liter. Vialed product was sterile and 1.7 +/- 0.4 mg/ml in PBS. Purity by SDS-PAGE was 99 +/- 1%. Aggregates by HPLC were <1%. Potency revealed a 24-h IC50 of 2.7 +/- 0.5 pM on HL60 cells. Endotoxin levels were 1 eu/mg. The N-terminal sequence was confirmed, and E. coli DNA was <113 pg/mg. The LD10 in mice was 110 microg/kg/day x5. There was no evidence of loss of solubility, proteolysis, aggregation, or loss of potency over 3 months at -80 and -20 degrees C. Further, the drug was stable at 4, 25, and 37 degrees C in human serum for 48 h. Drug reacted only with human monocytes, granulocytes, and myeloid precursors in frozen human tissue sections by immunohistochemistry. The synthesis of this protein drug should be useful for production for clinical phase I/II clinical trials and may be suitable for other diphtheria fusion toxins indicated for clinical development. This is the first report of the scaleup of a recombinant fusion toxin for clinical trials. Copyright 1999 Academic Press.
Tags: Animal; Human; Support, Non-U.S. Gov't; Support, U.S. Gov't, P.H.S. Descriptors: *Diphtheria Toxin--isolation and purification--IP; *Diphtheria Toxin--therapeutic use--TU; *Granulocyte-Macrophage Colony-Stimulating Factor--isolation and purification--IP; *Granulocyte-Macrophage Colony-Stimulating Factor--therapeutic use--TU; Acute Disease; Amino Acid Sequence; Base Sequence; DNA, Recombinant--genetics--GE; Diphtheria Toxin--genetics--GE; Drug Evaluation, Preclinical; Escherichia coli--genetics--GE; Gene Expression; Granulocyte-Macrophage Colony-Stimulat ing Factor--genetics--GE; HL-60 Cells; Lethal Dose 50; Leukemia, Myeloid --drug therapy--DT; Mice; Mice, Inbred C57BL; Molecular Sequence Data; Plasmids--genetics--GE; Recombinant Fusion Proteins --genetics--GE; Recombinant Fusion Proteins --isolation and purification--IP; Recombinant Fusion Proteins --therapeutic use--TU CAS Registry No.: 0 (DNA, Recombinant); 0 (Diphtheria Toxin); 0 (Plasmids); 0 (Recombinant Fusion Proteins); 83869-56-1 (Granulocyte-Macrophage Colony-Stimulating Factor)
Record Date Created: 19990712 Record Date Completed: 19990712

7/7/20 DIALOG(R)File 155:MEDLINE(R) (c) format only 2004 The Dialog Corp. All rts. reserv.
11814001 99253640 PMID: 10321723
Cloning and cytotoxicity of fusion proteins of EGF and angiogenin.
Yoon J M; Han S H; Kown O B; Kim S H; Park M H; Kim B K
Department of Microbial Chemistry, College of Pharmacy, Seoul National University, Kwanak-Gu, South Korea.
Life sciences (ENGLAND) 1999 , 64 (16) p1435-45, ISSN 0024-3205 Journal Code: 0375521 Document type: Journal Article Languages: ENGLISH Main Citation Owner: NLM Record type: Completed
Targeted toxins represent a new approach to specific cytocidal therapy. Immunotoxins based on plant and microbial toxins ar very immunogenic. To develop a targeted therapy that is less immunogenic and easily invades target tissues, four fusion prote containing human angiogenin targeted by human EGF have been constructed. EGF is a single chain polypeptide, which binds epidermal growth factor receptor (EGFR) and is known to be internalized by endocytosis. Angiogenin has been separately fus either at the amino terminus or the carboxyl terminus of EGF via linkers, giving rise to angiogenin-gly-EGF, angiogenin-(gly)4s EGF and EGF-angiogenin, EGF-gly-angiogenin, respectively. The fusion proteins were over-expressed in Escherichia coli and purified from periplasmic eluents by affinity chromatography. EGF-angiogenin and EGF-gly-angiogenin maintained receptor-binding activity of EGF and RNase activity of angiogenin in a single peptide and actively inhibited growth of human EGFR-positive target cells in culture. They are expected to have a very low immunogenic potential in humans because of their endogenous origin and also to have another potential therapeutic advantage because these fusion proteins may have overcom conventional immunotoxin and possess increased ability to penetrate because of their small size. Record Date Created: 19990526 Record Date Completed: 19990526

7/7/21
DIALOG(R)File 155:MEDLINE(R) (c) format only 2004 The Dialog Corp. All rts. reserv.
11799440 99238511 PMID: 10220447
Intranuclear delivery of an antiviral peptide mediated by the B subunit of Escherichia coli heat-labile enterotoxin.
Loregian A; Papini E; Satin B; Marsden H S; Hirst T R; Palu G
Institute of Microbiology, University of Padua, 35121 Padua, Italy.
Proceedings of the National Academy of Sciences of the United States of America (UNITED STATES) Apr 27 1999 , 96 (p5221-6, ISSN 0027-8424 Journal Code: 7505876 Document type: Journal Article Languages: ENGLISH
Main Citation Owner: NLM Record type: Completed
We report an intracellular peptide delivery system capable of targeting specific cellular compartments. In the model system w constructed a chimeric protein consisting of the nontoxic B subunit of Escherichia coli heat-labile enterotoxin (EtxB) fused to a 27-mer peptide derived from the DNA polymerase of herpes simplex virus 1. Viral DNA synthesis takes places in the nucleus a requires the interaction with an accessory factor, UL42, encoded by the virus. The peptide, designated Pol, is able to dissociat this interaction. The chimeric protein, EtxB-Pol, retained the functional properties of both EtxB and peptide components and w shown to inhibit viral DNA polymerase activity in vitro via disruption of the polymerase-UL42 complex. When added to virally infected cells, EtxB-Pol had no effect on adenovirus replication but specifically interfered with herpes simplex virus 1 replicatio Further studies showed that the antiviral peptide localized in the nucleus, whereas the EtxB component remained associated with vesicular compartments. The results indicate that the chimeric protein entered through endosomal acidic compartments a that the Pol peptide was cleaved from the chimeric protein before being translocated into the nucleus. The system we describe suitable for delivery of peptides that specifically disrupt protein-protein interactions and may be developed to target specific cellular compartments. Record Date Created: 19990610 Record Date Completed: 19990610

7/7/23 DIALOG(R)File 155:MEDLINE(R) (c) format only 2004 The Dialog Corp. All rts. reserv.
11775824 99214180 PMID: 10196187
A novel cytotoxin from Clostridium difficile serogroup F is a functional hybrid between two other large clostridial cytotoxins.
Chaves-Olarte E; Low P; Freer E; Norlin T; Weidmann M; von Eichel-Streiber C; Thelestam M
Microbiology and Tumorbiology Center, Karolinska Institutet, S-171 77 Stockholm, Sweden.
Journal of biological chemistry (UNITED STATES) Apr 16 1999 , 274 (16) p11046-52, ISSN 0021-9258 Journal Code: 2985121R Document type: Journal Article Languages: ENGLISH Main Citation Owner: NLM Record type: Completed
The large clostridial cytotoxins (LCTs) constitute a group of high molecular weight clostridial cytotoxins that inactivate cellular small GTP-binding proteins. We demonstrate that a novel LCT (TcdB-1470) from Clostridium difficile strain 1470 a functional hybrid between "reference" TcdB-10463 and Clostridium sordellii TcsL-1522. It bound to the same specific receptor as TcdB-10463 but glucosylated the same GTP-binding proteins as TcsL-1522. All three toxins had equal enzymatic potencies but were equally cytotoxic only when microinjected. When applied extracellularly TcdB-1470 and TcdB-10463 were considerably more potent cytotoxins than TcsL-1522. The small GTP-binding protein R-Ras was identified as a target for Tcd -1470 and also for TcsL-1522 but not for Tcd -10463. R-Ras is known to control integrin-extracellular mat

interactions from inside the cell. Its glucosylation may be a major determinant for the cell rounding and detachment induced by the two R-Ras-attacking toxins . In contrast, fibroblasts treated with TcdB-10463 were arborized and remained attached, with phosphotyrosine containing structures located at the cell-to-cell contacts and beta3-integrin remaining at the tips of cellular protrusions. These components were absent from cells treated with the R-Ras-inactivating toxins . The novel hybrid toxin will broaden the utility of the LCTs for clarifying the functions of several small GTPases, now including also R-Ras. Record Date Created: 19990517 Record Date Completed: 19990517

7/7/29 DIALOG(R)File 155:MEDLINE(R) (c) format only 2004 The Dialog Corp. All rts. reserv.
11747698 99185011 PMID: 10085027
Oligomerization of anthrax toxin protective antigen and binding of lethal factor during endocytic uptake into mammalian cells.
Singh Y; Klimpel K R; Goel S; Swain P K; Leppla S H
Centre for Biochemical Technology, Delhi 110007, India.
Infection and immunity (UNITED STATES) Apr 1999 , 67 (4) p1853-9, ISSN 0019-9567 Journal Code: 0246127
Document type: Journal Article Languages: ENGLISH Main Citation Owner: NLM Record type: Completed
The protective antigen (PA) protein of anthrax toxin binds to a cellular receptor and is cleaved by cell surface furin to produce a 63-kDa fragment (PA63). The receptor-bound PA63 oligomerizes to a heptamer and acts to translocate the catalytic moieties of the toxin, lethal factor (LF) and edema factor (EF), from endosomes to the cytosol. In this report, we used nondenaturing gel electrophoresis to show that each PA63 subunit in the heptamer can bind one LF molecule. Studies using PA immobilized on a plastic surface showed that monomeric PA63 is also able to bind LF. The internalization of PA and LF by cells was studied with radiolabeled and biotinylated proteins. Uptake was relatively slow, with a half-time of 30 min. The number of moles of LF internalized was nearly equal to the number of moles of PA subunit internalized. The essential role of PA oligomerization in LF translocation was shown with PA protein cleaved at residues 313-314. The oligomers formed by these proteins during uptake into cells were not as stable when subjected to heat and detergent as were those formed by native PA. The results show that the structure of the toxin proteins and the kinetics of proteolytic activation, LF binding, and internalization are balanced in a way that allows each PA63 subunit to internalize an LF molecule. This set of proteins has evolved to achieve highly efficient internalization and membrane translocation of the catalytic components, LF and EF. Record Date Created: 19990426 Record Date Completed: 19990426

7/7/31 DIALOG(R)File 155:MEDLINE(R) (c) format only 2004 The Dialog Corp. All rts. reserv.
11720993 99157583 PMID: 10048023
Expression and properties of an aerolysin--Clostridium septicum alpha toxin hybrid protein.
Diep D B; Nelson K L; Lawrence T S; Sellman B R; Tweten R K; Buckley J T
Department of Biochemistry and Microbiology, University of Victoria, BC, Canada.
Molecular microbiology (ENGLAND) Feb 1999 , 31 (3) p785-94, ISSN 0950-382X Journal Code: 8712028
Contract/Grant No.: AI37657; AI; NIAID Document type: Journal Article Languages: ENGLISH Main Citation Owner: NLM
Record type: Completed
Aerolysin is a bilobal channel-forming toxin secreted by Aeromonas hydrophila. The alpha toxin produced by Clostridium septicum is homologous to the large lobe of aerolysin. However, it does not contain a region corresponding to the small lobe of the Aeromonas toxin, leading us to ask what the function of the small lobe is. We fused the small lobe of aerolysin to alpha toxin, producing a hybrid protein that should structurally resemble aerolysin. Unlike aerolysin, the hybrid was not secreted when expressed in Aeromonas salmonicida. The purified hybrid was activated by proteolytic processing in the same way as both parent proteins and, after activation, it formed oligomers that corresponded to the aerolysin heptamer. Like aerolysin, the hybrid was far more active than alpha toxin against human erythrocytes and mouse T lymphocytes. Both aerolysin and the hybrid bound to human glycophorin, and both were inhibited by preincubation with this erythrocyte glycoprotein, whereas alpha toxin was unaffected. We conclude that aerolysin contains two receptor binding sites, one for glycosyl-phosphatidylinositol-anchored proteins that is located in the large lobe and is also found in alpha toxin, and a second site, located in the small lobe, that binds a surface carbohydrate determinant. Record Date Created: 19990506 Record Date Completed: 19990506

7/7/32 DIALOG(R)File 155:MEDLINE(R) (c) format only 2004 The Dialog Corp. All rts. reserv.
11720819 99157408 PMID: 10047878
Differential activity of cholera toxin and E. coli enterotoxin: construction and purification of mutant and hybrid derivatives.
Rodighiero C; Aman A T; Lencer W I; Hirst T R
University of Bristol, Department of Pathology and Microbiology, School of Medical Sciences, UK.
Biochemical Society transactions (ENGLAND) Nov 1998 , 26 (4) pS364, ISSN 0300-5127 Journal Code: 7506897
Document type: Journal Article Languages: ENGLISH Main Citation Owner: NLM Record type: Completed
Record Date Created: 19990413 Record Date Completed: 19990413

7/7/33 DIALOG(R)File 155:MEDLINE(R)(c) format only 2004 The Dialog Corp. All rts. reserv.
11680321 99115680 PMID: 9914159
The KDEL retrieval system is exploited by Pseudomonas exotoxin A, but not by Shiga-like toxin-1, during retrograde transport from the Golgi complex to the endoplasmic reticulum.
Jackson M E; Simpson J C; Girod A; Pepperkok R; Roberts L M; Lord J M
Department of Biological Sciences, University of Warwick, Coventry, CV4 7AL, UK. ml@dna.bio.warwick.ac.uk
Journal of cell science (ENGLAND) Feb 1999 , 112 (Pt 4) p467-75, ISSN 0021-9533 Journal Code: 0052457
Document type: Journal Article Languages: ENGLISH Main Citation Owner: NLM Record type: Completed
To investigate the role of the KDEL receptor in the retrieval of protein toxins to the mammalian cell endoplasmic reticulum (ER lysozyme variants containing AARL or KDEL C-terminal tags, or the human KDEL receptor, have been expressed in toxin-treated COS 7 and HeLa cells. Expression of the lysozyme variants and the KDEL receptor was confirmed by immunofluorescence. When such cells were challenged with diphtheria toxin (DT) or Escherichia coli Shiga-like toxin 1 (SLT-1 there was no observable difference in their sensitivities as compared to cells which did not express these exogenous proteins. contrast, the cytotoxicity of Pseudomonas exotoxin A (PE) is reduced by expressing lysozyme-KDEL, which causes a redistribution of the KDEL receptor from the Golgi complex to the ER, and cells are sensitised to this toxin when they express additional KDEL receptors. These data suggest that, in contrast to SLT-1, PE can exploit the KDEL receptor in order to reach ER lumen where it is believed that membrane transfer to the cytosol occurs. This contention was confirmed by microinjecting i Vero cells antibodies raised against the cytoplasmically exposed tail of the KDEL receptor. Immunofluorescence confirmed tha these antibodies prevented the retrograde transport of the KDEL receptor from the Golgi complex to the ER, and this in turn reduced the cytotoxicity of PE, but not that of SLT-1, to these cells. Record Date Created: 19990720 Record Date Completed: 19990720

7/7/36 DIALOG(R)File 155:MEDLINE(R) (c) format only 2004 The Dialog Corp. All rts. reserv.
11657978 99092760 PMID: 9876933
Stepwise transplantation of an active site loop between heat-labile enterotoxins LT-II and LT-I and characterization of the obtained hybrid toxins .
Feil I K; Platas A A; van den Akker F; Reddy R; Merritt E A; Storm D R; Hol W G
Howard Hughes Medical Institute, Department of Biological Structure, University of Washington, Seattle 98195-7742, USA
Protein engineering (ENGLAND) Nov 1998 , 11 (11) p1103-9, ISSN 0269-2139 Journal Code: 8801484
Contract/Grant No.: AI 34501; AI; NIAID Document type: Journal Article Languages: ENGLISH Main Citation Owner: NLM
Record type: Completed
Members of the cholera toxin family, including Escherichia coli heat-labile enterotoxins LT-I and LT-II, catalyze the covalent modification of intracellular proteins by transfer of ADP-ribose from NAD to a specific arginine of the target protein. The ADP-ribosylating activity of these toxins is located in the A-subunit, for which LT-I and LT-II share a 63% sequence identity. The flexible loop in LT-I, ranging from residue 47 to 56, closes over the active site cleft. Previous studies have shown that point mutations in this loop have dramatic effects on the activity of LT-I. Yet, in LT-II the sequence of the equivalent loop differs at fo positions from LT-I. Therefore five mutants of the active site loop were created by a stepwise replacement of the loop sequenc in LT-I with virtually all the corresponding residues in LT-II. Since we discovered that LT-II had no activity versus the artificial substrate diethylamino-benzylidine-aminoguan idine (DEABAG) while LT-I does, our active site mutants most likely probe the NAD binding, not the arginine binding region of the active site. The five hybrid toxins obtained (Q49A, F52N, V53T, Q49V/F52 and Q49V/F52N/V53T) show (i) great differences in holotoxin assembly efficiency; (ii) decreased cytotoxicity in Chinese hams ovary cells; and (iii) increased in vitro enzymatic activity compared with wild type LT-I. Specifically, the three mutants containin the F52N substitution display a greater Vmax for NAD than wild type LT-I. The enzymatic activity of the V53T mutant is significantly higher than that of wild type LT-I. Apparently this subtle variation at position 53 is beneficial, in contrast to several other substitutions at position 53 which previously had been shown to be deleterious for activity. The most striking result of this study is that the active site loop of LT-I, despite great sensitivity for point mutations, can essentially be replaced by the active s loop of LT-II, yielding an active 'hybrid enzyme' as well as 'hybrid toxin'. Record Date Created: 19990308 Record Date Completed: 19990308

7/7/38 DIALOG(R)File 155:MEDLINE(R) (c) format only 2004 The Dialog Corp. All rts. reserv.
11626571 99060051 PMID: 9843379
Characterization of membrane translocation by anthrax protective antigen.
Wesche J; Elliott J L; Falnes P O; Olsnes S; Collier R J
Department of Microbiology and Molecular Genetics, Harvard Medical School, Boston, Massachusetts 02115, USA.
Biochemistry (UNITED STATES) Nov 10 1998 , 37 (45) p15737-46, ISSN 0006-2960 Journal Code: 0370623
Contract/Grant No.: AI22021; AI; NIAID Document type: Journal Article Languages: ENGLISH Main Citation Owner: NLM
Record type: Completed
Solving the crystallographic structure of the ring-shaped heptamer formed by protective antigen (PA), the B moiety of anthrax toxin, has focused attention on understanding how this oligomer mediates membrane translocation of the toxin's A moieties. W have developed an assay for translocation in which radiolabeled ligands are bound to proteolytically activated PA (PA63) at th surface of CHO or L6 cells, and translocation across the plasma membrane is induced by lowering the pH. The cells are then treated with Pronase E to degrade residual surface-bound material, and protected ligands are quantified after fractionation by SDS-PAGE. Translocation was most efficient (35%-50%) with LFN, the N-terminal PA binding domain of the anthrax lethal fac (LF). Intact LF, edema factor (EF), or fusion proteins containing LFN fused to certain heterologous proteins [the diphtheria toxi A chain (DTA) or dihydrofolate reductase (DHFR)] were less efficiently translocated (15%-20%); and LFN fusions to several other proteins were not translocated at all. LFN with different N-terminal residues was found to be degraded according to the N end rule by the proteasome, and translocation of LFN fused to a mutant form of DHFR with a low affinity for methotrexate (MT

protected cells from the effects of MTX. Both results are consistent with a cytosolic location of protected proteins. Evidence that a protein must unfold to be translocated was obtained in experiments showing that (i) translocation of LFNDTA was blocked by introduction of an artificial disulfide into the DTA moiety, and (ii) translocation of LFNDHFR and LFNDTA was blocked by their ligands (MTX and adenine, respectively). These results demonstrate that the acid-induced translocation by anthrax toxin closely resembles that of diphtheria toxin, despite the fact that these two toxins are unrelated and form pores by different mechanisms. Record Date Created: 19981221 Record Date Completed: 19981221

7/7/39 DIALOG(R)File 155:MEDLINE(R) (c) format only 2004 The Dialog Corp. All rts. reserv.
11606274 99039034 PMID: 9821593
Positive selection vectors to generate fused genes for the expression of his-tagged proteins.
Van Reeth T; Dreze P L; Szpirer J; Szpirer C; Gabant P
Universite Libre de Bruxelles, Rhode-Saint-Genese, Belgium.
BioTechniques (UNITED STATES) Nov 1998 , 25 (5) p898-904, ISSN 0736-6205 Journal Code: 8306785
Document type: Journal Article Languages: ENGLISH Main Citation Owner: NLM Record type: Completed
Epitope tagging simplifies detection, characterization and purification of proteins. Gene fusion to combine the coding region of a well-characterized epitope with the coding region for a protein of interest generally requires several subcloning steps. Alternatively, a PCR strategy can be used to generate such a chimeric gene. In addition to its simplicity, this approach allows one to limit the size of the multiple cloning sites present in conventional expression vectors, thus reducing the introduction of artifactual amino-acid sequences into the fused protein. In this communication, we describe new vectors that allow PCR cloning and selection of chimeric genes coding for N- or C-terminal His-tagged proteins. These vectors are based on the control of cell death CcdB direct selection technology and are well adapted to the cloning of blunt-ended PCR products that were generated by using thermostable polymerases that provide proofreading activity. Record Date Created: 19990119 Record Date Completed: 19990119

7/5/52 DIALOG(R)File 155:MEDLINE(R) (c) format only 2004 The Dialog Corp. All rts. reserv.
11368068 98248937 PMID: 9587366
Recombinant immunotoxins and chimeric toxins for targeted therapy in oncology]
Immunotoxines recombinantes et toxines chimeres pour une therapie ciblee en oncologie.
Chiron M F
Rhone-Poulenc Rorer Gencell, Centre de recherche de Vitry-Alfortville, France.
Bulletin du cancer (FRANCE) Dec 1997 , 84 (12) p1135-40, ISSN 0007-4551 Journal Code: 0072416
Document type: Journal Article; Review; Review, Tutorial ; English Abstract Languages: FRENCH
Main Citation Owner: NLM Record type: Completed Subfile: INDEX MEDICUS
Immunotoxins and chimeric toxins are hybrid molecules constituted of antibodies, growth factor or cytokines coupled to peptide toxins . They are designed to selectively eliminate tumor cells. Some of these chimera have been shown to induce complete tumor regressions of human tumor xenografts in immunodeficient mice. In clinical trials, higher anti tumor response were observed in lymphoma, brain tumor, breast and colon cancers. Problems arose with normal tissue toxicity and the production of neutralising antibodies. Should the latest recombinant toxins conceived by rationale designed, solved these problems, chimeric toxins would be an alternative approach to target tumor cells and vascular endothelial cells in solid tumors. (37 Refs.)
Tags: Animal; Human Descriptors: Antigen-Presenting Cells--drug effects--DE; *Immunotoxins --therapeutic use--TU; *Neoplasms, Experimental--therapy--TH; * Recombinant Fusion Proteins --therapeutic use--TU; Antibodies, Monoclonal--pharmacology --PD; Antibodies, Monoclonal--therapeutic use--TU; Bacterial Toxins --pharmacology--PD; Bacterial Toxins --therapeutic use--TU; Cytotoxicity, Immunologic; Exotoxins--pharmacology--PD; Exotoxins--therapeutic use--TU; Immunotherapy--methods--MT; Immunotoxins--pharmacology--PD; Immunotoxins --toxicity--TO; Mice; Recombinant Fusion Proteins --pharmacology--PD; Recombinant Fusion Proteins --toxicity--TO CAS Registry No.: 0 (Antibodies, Monoclonal); 0 (Bacterial Toxins); 0 (Exotoxins); 0 (Immunotoxins); 0 (Recombinant Fusion Proteins)
Record Date Created: 19980602 Record Date Completed: 19980602

7/5/55 DIALOG(R)File 155:MEDLINE(R) (c) format only 2004 The Dialog Corp. All rts. reserv.
11337192 98217169 PMID: 9558086
Increasing immunogenicity of antigens fused to Ig-binding proteins by cell surface targeting.
Leonetti M; Thai R; Cotton J; Leroy S; Drevet P; Ducancel F; Boulain J C; Menez A
Departement d'Ingenierie et d'Etudes des Proteines, C. E. Saclay, Gif-Sur-Yvette, France. leonetti@cea.fr
Journal of immunology (Baltimore, Md. - 1950) (UNITED STATES) Apr 15 1998 , 160 (8) p3820-7, ISSN 0022-1767 Journal Code: 2985117R Document type: Journal Article Languages: ENGLISH Main Citation Owner: NLM
Record type: Completed Subfile: AIM; INDEX MEDICUS
Fusion of antigenic proteins to Ig-binding proteins such as protein A from Staphylococcus aureus and its derived ZZ fragment is known to increase immunogenicity of the fused Ag in vivo. To shed light on the origin of this effect, we used snake toxins as Ags and observed that 1) fusion of toxins to ZZ enhanced their presentation to a toxin-specific T cell hybridoma (T1B2), using A20 B lymphoma cells, splenocytes, or peritoneal exudate cells as APCs; 2) this enhancement further increased when the number of fused Ig-binding domains varied from two with ZZ to five with protein A; and 3) the phenomenon vanished when the fusion protein was preincubated with an excess of free ZZ or when P388D1 monocytes cells were used as APCs. Therefore, ZZ-fused toxins are likely to be targeted to surface Igs of APCs by their ZZ moiety. Furthermore, ZZ-alpha and toxin alpha stimulated similar profiles of toxin-specific T cells in BALB/c mice, suggesting a comparable processing and presentation in vivo for both toxin forms. To improve the targeting efficiency, ZZ-alpha was noncovalently complexed to various Igs directed to different cel surface components of APCs. The resulting complexes were up to 10(3)-fold more potent than the free toxin at stimulating T1B Also, they elicited both a T cell and an Ab response in BALB/c mice, without the need of any adjuvant. This simple approach m find practical applications by increasing the immunogenicity of recombinant proteins without the use of adjuvant.
Tags: Animal; In Vitro Descriptors: Antigens--metabolism--ME; *Carrier Proteins--immunology--IM; *Carrier Proteins--metabolism--ME; *Immunoglobulins--metabolism--ME; * Recombinant Fusion Proteins --immunology--IM; * Recombinant Fusion Proteins --metabolism--ME Antibody Formation; Antigen Presentation; Antigen-Presenting Cells--immunology--IM; Cell Membrane--immunology--IM; Erabutoxins--immunology--IM; Hybridomas; Immunization; Lymphocyte Activation; Mice; Mice, Inbred BALB C; Peptide Fragments--immunology--IM; Pep Fragments--metabolism--ME; Staphylococcal Protein A--immunology --IM; Staphylococcal Protein A--metabolism--ME; T-Lymphocytes--immunology --IM CAS Registry No.: 0 (Antigens); 0 (Carrier Proteins); 0 (Erabutoxins); 0 (Immunoglobulins); 0 (Peptide Fragments); 0 (Recombinant Fusion Proteins); 0 (Staphylococcal Protein A); 11094-61-4 (erabutoxin A)
Record Date Created: 19980504 Record Date Completed: 19980504

7/7/63 DIALOG(R)File 155:MEDLINE(R) (c) format only 2004 The Dialog Corp. All rts. reserv.
11274724 98153210 PMID: 9485477
Cytotoxicity and specificity of directed toxins composed of diphtheria toxin and the EGF-like domain of heregulin beta1.
Landgraf R; Pegram M; Slamon D J; Eisenberg D
Department of Chemistry and Biochemistry and Division of Hematology-Oncology, University of California--Los Angeles, Box 951570, Los Angeles, California 90095-1570, USA.
Biochemistry (UNITED STATES) Mar 3 1998 , 37 (9) p3220-8, ISSN 0006-2960 Journal Code: 0370623
Contract/Grant No.: 1K12 CA01714; CA; NCI; GM31299; GM; NIGMS Document type: Journal Article
Languages: ENGLISH Main Citation Owner: NLM Record type: Completed
As a step in the design of directed toxins , aimed at cells that overexpress HER receptors, particularly breast carcinoma cells, we studied the properties of a chimera of diphtheria toxin (DT) and heregulin beta1. The EGF-like growth hormone heregulin is ligand for the HER3 and HER4 receptors and their heterodimers with HER2. The 60-residue EGF-like domain (hrg) of heregul elicits a biological response and binds to these receptors primarily through its N terminus. We tested a fusion protein in which replaces the C-terminal receptor-binding domain of DT (DT(389)hrg) and an alternative design in which this domain is fused to the N terminus of DT(389). Of those two constructs, the N-terminal fusion was not active as a directed toxin but elicited a grow response. The C-terminal fusion of hrg to DT(389) yielded a functional toxin and showed cell line specific cytotoxicity that is consistent with heregulin specificity. The binding of hrg to its cognate receptor is not impaired as shown by receptor activation direct binding, and competition with free hrg. Cytotoxicity is dependent on high-affinity binding of DT(389)hrg to HER3 and HE receptors and is not mediated by HER2 overexpression alone. For those cell lines exhibiting high-affinity binding sites, the leve of cytotoxicity correlates with the rate of internalization. Thus DT(389)hrg chimeras offer a possible avenue toward directed toxins against cells that overexpress HER receptors. Record Date Created: 19980403 Record Date Completed: 19980403

7/7/65 DIALOG(R)File 155:MEDLINE(R) (c) format only 2004 The Dialog Corp. All rts. reserv.
11269315 98147722 PMID: 9488398
Chimeric clostridial cytotoxins: identification of the N-terminal region involved in protein substrate recognition.
Hofmann F; Busch C; Aktories K
Institut fur Pharmakologie und Toxikologie der Albert-Ludwigs-Universitat Freiburg, Germany.
Infection and immunity (UNITED STATES) Mar 1998 , 66 (3) p1076-81, ISSN 0019-9567 Journal Code: 0246127
Document type: Journal Article Languages: ENGLISH Main Citation Owner: NLM Record type: Completed
Clostridium sordellii lethal toxin is a member of the family of large clostridial cytotoxins that glucosylate small GTPases. In contrast to Clostridium difficile toxins A and B, which exclusively modify Rho subfamily proteins, C. sordellii lethal toxin also glucosylates Ras subfamily proteins. By deletion analysis and construction of chimeric fusion proteins of C. sordellii lethal toxin and C. difficile toxin B, we localized the enzyme activity of the lethal toxin to the N terminus of the holotoxin and identified the region involved in protein substrate specificity. The toxin fragment of the N-terminal 546 amino acid residues of C. sordellii leth toxin glucosylated Rho and Ras subfamily proteins, as the holotoxin did. Deletion of a further 30 amino acid residues from the terminus of this active fragment drastically reduced glucotransferase activity and blocked glucohydrolase activity. Exchange of amino acid residues 364 through 516 of lethal toxin for those in the active toxin B fragment (1 to 546) allowed glucosylation of Ras subfamily proteins. In contrast, the chimera with amino acids 1 to 364 from toxin B, 365 to 468 from lethal toxin, and 469 t 546 from toxin B exhibited markedly reduced modification of Ras subfamily proteins, whereas modification of Rac and Cdc42 was hardly changed. The data indicate that the region of amino acid residues 364 through 516 primarily defines the substrate specificity of C. sordellii lethal toxin. Record Date Created: 19980312 Record Date Completed: 19980312

7/7/92 DIALOG(R)File 155:MEDLINE(R) (c) format only 2004 The Dialog Corp. All rts. reserv.
10866676 97218154 PMID: 9065815
In vitro effects of a recombinant toxin, mSCF-PE40, targeting c-kit receptors ectopically expressed in small cell lung cancers.
Nishida K; Seto M; Takahashi T; Oshima Y; Asano S; Tojo A; Ueda R
Laboratory of Chemotherapy, Aichi Cancer Center Research Institute, Nagoya, Japan.
Cancer letters (IRELAND) Feb 26 1997 , 113 (1-2) p153-8, ISSN 0304-3835 Journal Code: 7600053
Document type: Journal Article Languages: ENGLISH Main Citation Owner: NLM Record type: Completed

Most small cell lung cancers (SCLCs) ectopically express high levels of the c-kit receptor. We have examined if the receptor can serve as a target for a chimeric toxin, mSCF-PE40 composed of murine stem cell factor (SCF) genetically fused to the N terminus of a modified form of Pseudomonas exotoxin (PE) lacking its cell recognition domain. Selective cytotoxicity was found for human c-kit receptor-negative cells. This agent thus warrants further evaluation for therapy of human CSLCs. Record Date Created: 19970407 Record Date Completed: 19970407

7/7/96 DIALOG(R)File 155:MEDLINE(R) (c) format only 2004 The Dialog Corp. All rts. reserv.
10819657 97109543 PMID: 8951823
Pseudomonas exotoxin exhibits increased sensitivity to furin when sequences at the cleavage site are mutated to resemble the arginine-rich loop of diphtheria toxin.
Chiron M F; Ogata M; FitzGerald D J
Biotherapy Section, National Cancer Institute, National Institutes of Health, Bethesda, Maryland 20892, USA.
Molecular microbiology (ENGLAND) Nov 1996 , 22 (4) p769-78, ISSN 0950-382X Journal Code: 8712028
Document type: Journal Article Languages: ENGLISH Main Citation Owner: NLM Record type: Completed
To be toxic for mammalian cells, Pseudomonas exotoxin (PE) requires proteolytic cleavage between Arg-279 and Gly-280. Cleavage, which is mediated by the cellular protease furin, generates an active C-terminal fragment which translocates to the cytosol and inhibits protein synthesis. In vitro, furin-mediated cleavage is optimal at pH 5.5 with a relatively slow turnover rate. Within cells, only 5-10% of cell-associated PE is cleaved. To investigate the reasons for this inefficient cleavage, the amino acid composition near the cleavage site was altered to resemble more closely the arginine-rich sequence from the functionally similar region of diphtheria toxin (DT). Four PE-DT mutants were generated, whereby 1, 5, 6 or 8 amino acids at the PE-cleavage site were changed to amino acids found at the DT-cleavage site. Mutant proteins were expressed in Escherichia coli, purified and then analysed for their susceptibility to cleavage by furin and trypsin, susceptibility to cell-mediated cleavage, and cytotoxic activity relative to wild-type PE. At pH 5.5, the rate of both furin-mediated cleavage and trypsin-mediated cleavage increased dramatically when amino acids in PE were altered to resemble the DT sequence. This increase did not alter the pH optimum for furin-mediated cleavage of PE toxins , which remained at pH 5.0-5.5. When radioactive versions of selected PE-DT proteins were added to intact cells, an increase in the percentage of molecules that were cleaved relative to wild-type PE was also seen. However, changes that favoured increased proteolysis apparently interfered with other important toxin functions because none of the PE-DT proteins exhibited enhanced toxicity for cells when compared with the activity of wild-type PE. Record Date Created: 19970331 Record Date Completed: 19970331

10/6/1 14406705 22309410 PMID: 12421321
SycE allows secretion of YopE-DHFR hybrids by the Yersinia enterocolitica type III Ysc system. Nov 2002

10/6/2 11633291 99067023 PMID: 9851698
Determinants of the fidelity of processing glucoamylase-lysozyme fusions by Aspergillus niger. Nov 15 1998

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Status of YopM and YopN in the Yersinia Yop virulon: YopM of Y.enterocolitica is internalized inside the cytosol of PU5-1.8 macrophages by the YopB, D, N delivery apparatus. Oct 1 1996

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Purification of recombinant human epidermal growth factor secreted from the methylotrophic yeast Hansenula polymorpha. Feb 2002

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The type III secretion chaperone LcrH co-operates with YopD to establish a negative, regulatory loop for control of Yop synthesis in Yersinia pseudotuberculosis. Nov 2001

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The lcrB (yscN/U) gene cluster of Yersinia pseudotuberculosis is involved in Yop secretion and shows high homology to the spa gene clusters of Shigella flexneri and Salmonella typhimurium. May 1994

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Purification and characterization of the trefoil peptide human spasmolytic polypeptide (hSP) produced in yeast. Mar 8 1993

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Efficient secretion in yeast based on fragments from K1 killer preprotoxin. Apr 1992

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Structure and regulation of the Yersinia pestis yscBCDEF operon. Jul 1992

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Regulation of alpha-factor production in Saccharomyces cerevisiae: a-factor pheromone-induced expression of the MF alpha 1 and STE13 genes. Oct 1989

10/5/7 DIALOG(R)File 155:MEDLINE(R) (c) format only 2004 The Dialog Corp. All rts. reserv.
07723384 93178658 PMID: 8440393
Purification and characterization of the trefoil peptide human spasmolytic polypeptide (hSP) produced in yeast.
Thim L; Norris K; Norris F; Nielsen P F; Bjorn S E; Christensen M; Petersen J
Department of Protein Chemistry, Pharmaceuticals Research, Novo Nordisk, Novo Alle, Bagsvaerd, Denmark.
FEBS letters (NETHERLANDS) Mar 8 1993, 318 (3) p345-52, ISSN 0014-5793 Journal Code: 0155157
Document type: Journal Article Languages: ENGLISH Main Citation Owner: NLM Record type: Completed
Subfile: INDEX MEDICUS
Recombinant human spasmolytic polypeptide (r-hSP) has been produced in relatively large amounts in Saccharomyces cerevisiae. The two intronless trefoil domains of the hSP-DNA were cloned separately by PCR from human genomic DNA, and the remaining parts of the gene synthesized. Recombinant plasmids were constructed to encode a fusion protein consisting of hybrid leader sequence and the hSP sequence. The leader sequence serves to direct the fusion protein into the secretory pathway of the cell and to expose it to the Kex 2 processing enzyme system. The secreted r-hSP was found in a glycosylated and an non-glycosylated form. The two forms of r-hSP were purified from the yeast fermentation broth by a combination of ion exchange chromatography and preparative HPLC. The overall yield from 8 litres of fermentation broth was 160 mg r-hSP and 219 mg glycosylated r-hSP corresponding to 50% and 34%, respectively. The structure of the r-hSP and the glycosylated r-hS was determined by amino acid analysis and carbohydrate composition analysis as well as by peptide mapping, amino acid sequencing and mass spectrometric analysis.
Tags: Human Descriptors: Peptides--isolation and purification--IP; * Recombinant Fusion Proteins --isolation and purification--IP; *Saccharomyces cerevisiae --metabolism--ME; Amino Acid Sequence; Amino Acids--analysis--AN; Base Sequence; Carbohydrates--analysis AN; Chromatography, High Pressure Liquid ; Chromatography, Ion Exchange; Cloning, Molecular; DNA--genetics--GE; Glycosylation; Growt Substances--chemistry--CH; Growth Substances --genetics--GE; Molecular Sequence Data; Peptide Mapping; Peptides --chemistry--CH; Peptides--genetics--GE; Plasmids; Polymerase Chain Reaction; Recombinant Fusion Proteins --biosynthesis--BI; Recombinant Fusion Proteins --chemistry--CH; Saccharomyces cerevisiae--genetics--GE; Spectrum Analysis, Mass CAS Registry No.: 0 (Amino Acids); 0 (Carbohydrates); 0 (Growth Substances); 0 (Peptides); 0 (Plasmids); 0 (Recombinant Fusion Proteins); 146046-78-8 (trefoil factor); 8298 77-7 (pancreatic spasmolytic polypeptide); 9007-49-2 (DNA)
Record Date Created: 19930330 Record Date Completed: 19930330

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Targeting HIV proteins to the major histocompatibility complex class I processing pathway with a novel gp120-anthrax toxin fusion protein. Oct 2 1997

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Identification and characterization of an extracellular protease activity produced by the marine Vibrio sp. 60. Feb 1 1996

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Role of processing and intracellular transport for optimal toxicity of Shiga toxin and toxin mutants. May 1995

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Proteolytic cleavage at arginine residues within the hydrophilic disulphide loop of the Escherichia coli Shiga-like toxin I A subunit is not essential for cytotoxicity. Oct 1993

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Genetic identification of exported proteins in Streptococcus pneumoniae. Sep 1993

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Expression of the Pasteurella haemolytica leukotoxin is inhibited by a locus that encodes an ATP-binding cassette homolog. Sep 1993

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Secretion of CyaA-PrtB and HlyA-PrtB fusion proteins in Escherichia coli: involvement of the glycine-rich repeat domain of Erwinia chrysanthemi protease B. Aug 1992

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Association of degradation and secretion of three chimeric polypeptides in Escherichia coli. May 1988

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The gamma-secretase-generated intracellular domain of beta-amyloid precursor protein binds Numb and inhibits Notch signaling. May 14 2

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SecA-dependence of the translocation of a large periplasmic loop in the Escherichia coli MalF inner membrane protein is a function of sequence context. Apr-Jun 1995

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Why green fluorescent fusion proteins have not been observed in the vacuoles of higher plants. Aug 2003

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UDP-galactose:ceramide galactosyltransferase is a class I integral membrane protein of the endoplasmic reticulum. Oct 2 1998

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Prodomain-dependent nuclear localization of the caspase-2 (Nedd2) precursor. A novel function for a caspase prodomain. Sep 18 1998

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Anionic phospholipids are determinants of membrane protein topology. Jul 16 1997

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Ricin A chain fused to a chloroplast-targeting signal is unfolded on the chloroplast surface prior to import across the envelope membranes. Feb 23 1996

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Proteasome inhibitors block VCAM-1 and ICAM-1 gene expression in endothelial cells without affecting nuclear translocation of nuclear factor-kappa B. Apr 1996

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Signal transduction by activated mNotch: importance of proteolytic processing and its regulation by the extracellular domain. Feb 20 1996

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Rapid transmembrane movement of C6-NBD-labeled phospholipids across the inner membrane of Escherichia coli. Apr 3 1996

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Topological characterization of the essential Escherichia coli cell division protein FtsN. Mar 1996

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Analysing c-kit internalization using a functional c-kit-EGFP chimera containing the fluorochrome within the extracellular domain. Jul 4 2002

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Hypoxia-inducible factor-1 alpha (HIF-1 alpha) escapes O(2)-driven proteasomal degradation irrespective of its subcellular localization: nucleus or cytoplasm. Jul 2001

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Ligand-dependent degradation of Smad3 by a ubiquitin ligase complex of ROC1 and associated proteins. May 2001

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The human peroxisomal targeting signal receptor, Pex5p, is translocated into the peroxisomal matrix and recycled to the cytosol. Apr 20 2001

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The nucleoporin Nup98 associates with the intranuclear filamentous protein network of TPR. Mar 13 2001

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Proteasome inhibition induces nuclear translocation and transcriptional activation of the dioxin receptor in mouse embryo primary fibroblasts the absence of xenobiotics. Mar 2001

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The amino-terminal domain of apolipoprotein B does not undergo retrograde translocation from the endoplasmic reticulum to the cytosol. Proteasomal degradation of nascent apolipoprotein B begins at the carboxyl terminus of the protein, while apolipoprotein B is still in its original translocon. Oct 13 2000

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Characterization of the signal that directs Tom20 to the mitochondrial outer membrane. Oct 16 2000

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C-terminal glycine-histidine tagging of the outer membrane protein lga beta of Neisseria gonorrhoeae. Apr 1 1995

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Import of transcription factor MTF1 into the yeast mitochondria takes place through an unusual pathway. May 19 1995

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Proteolytic cleavage at arginine residues within the hydrophilic disulphide loop of the Escherichia coli Shiga-like toxin I A subunit is not essential for cytotoxicity. Oct 1993

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Molecular chaperones cooperate with PIM1 protease in the degradation of misfolded proteins in mitochondria. Nov 1 1994

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Genetic identification of exported proteins in Streptococcus pneumoniae. Sep 1993

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Translocation of N-terminal tails across the plasma membrane. Oct 3 1994

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Carboxyl-terminal sequences can influence the in vitro import and intraorganellar targeting of chloroplast protein precursors. Jul 15 1992

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Selective extracellular release of cholera toxin B subunit by Escherichia coli: dissection of Neisseria Iga beta-mediated outer membrane transport. Jun 1992

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Cytochromes c1 and b2 are sorted to the intermembrane space of yeast mitochondria by a stop-transfer mechanism. May 29 1992

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Protein import into the yeast mitochondrial matrix. A new translocation intermediate between the two mitochondrial membranes. Nov 5 1991

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Aberrant mitochondrial processing of chimaeric import precursors containing subunits 8 and 9 of yeast mitochondrial ATP synthase. Dec 1990

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SecY, a multispanning integral membrane protein, contains a potential leader peptidase cleavage site. Jun 1990

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Topogenic analysis of the human immunodeficiency virus type 1 envelope glycoprotein, gp160, in microsomal membranes. Nov 1988

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Signal and membrane anchor functions overlap in the type II membrane protein I gamma CAT. Jun 1988

18/7/20 DIALOG(R)File 155:MEDLINE(R) (c) format only 2004 The Dialog Corp. All rts. reserv.
10396906 96202337 PMID: 8643690
Signal transduction by activated mNotch: importance of proteolytic processing and its regulation by the extracellular domain.
Kopan R; Schroeter E H; Weintraub H; Nye J S
Division of Dermatology, Department of Molecular Biology and Pharmacology, Washington University, St. Louis, MO 63110, USA.
Proceedings of the National Academy of Sciences of the United States of America (UNITED STATES) Feb 20 1996, 93 (4) p1683-8, ISSN 0027-8424 Journal Code: 7505876 Document type: Journal Article Languages: ENGLISH
Main Citation Owner: NLM Record type: Completed
Previous studies imply that the intracellular domain of Notch1 must translocate to the nucleus for its activity. In this study, we demonstrate that a mNotch1 mutant protein that lacks its extracellular domain but retains its membrane-spanning region becomes proteolytically processed on its intracellular surface and, as a result, the activated intracellular domain (mNotchIC) is released and can move to the nucleus. Proteolytic cleavage at an intracellular site is blocked by protease inhibitors. Intracellular cleavage is not seen in cells transfected with an inactive variant, which includes the extracellular lin-Notch-glp repeats. Collectively, the studies presented here support the model that mNotch1 is proteolytically processed and the cleavage product is translocated to the nucleus for mNotch1 signal transduction. Record Date Created: 19960717 Record Date Completed: 19960717

18/7/21 DIALOG(R)File 155:MEDLINE(R) (c) format only 2004 The Dialog Corp. All rts. reserv.
10394860 96200283 PMID: 8634315
Rapid transmembrane movement of C6-NBD-labeled phospholipids across the inner membrane of Escherichia coli.
Huijbregts R P; de Kroon A I; de Kruijff B
Department Biochemistry of Membranes, Centre for Biomembranes and Lipid Enzymology, Institute of Biomembranes, Utrecht University, The Netherlands.
Biochimica et biophysica acta (NETHERLANDS) Apr 3 1996, 1280 (1) p41-50, ISSN 0006-3002 Journal Code: 0217513 Document type: Journal Article Languages: ENGLISH Main Citation Owner: NLM Record type: Completed
In this study we have investigated the transmembrane movement of short chain fluorescently labeled phospholipids across the inner membrane of Escherichia coli. Exogenously added C6-NBD-labeled phospholipids rapidly flip across the inner membrane of E. coli, as was shown by a dithionite reduction assay applied to inverted inner membrane vesicles (IIMV) isolated from wild type E. coli cells. The rate of transmembrane movement of the phospholipid probes incorporated into IIMV is temperature dependent, and shows no phospholipid head group specificity. C6-NBD-labeled phospholipids translocate across the membrane of IIMV incubated at 37 degrees C with a t1/2 of 7 min. After the incorporation into IIMV C6-NBD-PG is partially converted to CL by CL-synthase. If IIMV are pretreated with proteinase K the conversion of this fluorescent probe to C6-NBD-CL is not observed anymore, suggesting that the catalytic domain of CL-synthase is at the cytoplasmic site of the plasma membrane of E. coli. Newly synthesized C6-NBD-CL also flips across the inner membrane although at a slower rate than the other phospholipid probes. The transmembrane movement occurs in both directions and is not influenced by treatment of the IIMV with a sulfhydryl reagent or a proteinase, nor by the presence of ATP, or a deltapH across the membrane of the IIMV. However, the transmembrane movement of the C6-NBD-labeled phospholipid probes is not observed in LUVETs (large unilamellar vesicles made by extrusion technique) prepared of wild type E. coli lipids, indicating that the rapid transmembrane movement of phospholipids across the inner membrane of E. coli is a protein-mediated process. Record Date Created: 19960710 Record Date Completed: 19960710

18/7/35 DIALOG(R)File 155:MEDLINE(R) (c) format only 2004 The Dialog Corp. All rts. reserv.
08370202 95058175 PMID: 7968513
Proteolytic cleavage at arginine residues within the hydrophilic disulphide loop of the Escherichia coli Shiga-like toxin I A subunit is not essential for cytotoxicity.
Burgess B J; Roberts L M
Department of Biological Sciences, University of Warwick, Coventry, UK.
Molecular microbiology (ENGLAND) Oct 1993, 10 (1) p171-9, ISSN 0950-382X Journal Code: 8712028
Document type: Journal Article Languages: ENGLISH Main Citation Owner: NLM Record type: Completed
Escherichia coli Shiga-like toxin I is a type II ribosome-inactivating protein composed of an A subunit with RNA-specific N-glycosidase activity, non-covalently associated with a pentamer of B subunits possessing affinity for galabiose-containing glycolipids. The A subunit contains a single intrachain disulphide bond encompassing a hydrophilic sequence containing two trypsin-sensitive arginine residues. By analogy with other bacterial toxins it has been proposed that proteolytic nicking, deeme essential for a cytotoxic effect, occurs within this disulphide-bonded loop to generate the A1 and A2 fragments. Reduced A1 is then believed to translocate an internal membrane to inactivate protein synthesis in the cytosol. In this report, the disulphide-lo arginines of the SLT I A subunit were mutated to block the specific proteolysis presumed to occur. However, the mutant generated remained an effective toxin having similar catalytic activity to wild-type toxin and only a marginally reduced cytotoxic towards cultured cells. We conclude that the disulphide-loop arginine residues are not the unique and essential processing site previously assumed, but that processing may occur at alternative accessible sites to compensate for loss of target sites within the loop. Record Date Created: 19941129 Record Date Completed: 19941129

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Regulating the conducting states of a mammalian serotonin transporter. Oct 30 2003

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Rho-specific Bacillus cereus ADP-ribosyltransferase C3cer cloning and characterization. Aug 19 2003

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Expression, purification, and efficacy of the type A botulinum neurotoxin catalytic domain fused to two translocation domain variants. May 2003

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Entrapment of Rho ADP-ribosylated by Clostridium botulinum C3 exoenzyme in the Rho-guanine nucleotide dissociation inhibitor-1 complex. 05 2003

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Reversible suppression of glutamatergic neurotransmission of cerebellar granule cells in vivo by genetically manipulated expression of tetanus neurotoxin light chain. Jul 30 2003

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Intera ctions between synaptic vesicle fusion proteins explored by atomicforce microscopy. 07 09 2003

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Prostaglandin F(2alpha) stimulation of cyclooxygenase-2 promoter activity by the FP(B) prostanoid receptor. Mar 28 2003

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Channel formation by the binding component of Clostridium botulinum C2 toxin: glutamate 307 of C2II affects channel properties in vitro a pH-dependent C2I translocation in vivo. May 13 2003

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A sing le dose of recombinant Salmonella typhimurium induces specific humoral immune responses against heterologous Eimeria tenella antigens in chicken. Jan 2003

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The uptake machinery of clostridial actin ADP-ribosylating toxins--a cell delivery system for fusion proteins and polypeptide drugs. 09 24 2002

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The Rho/ROCK pathway mediates neurite growth-inhibitory activity associated with the chondroitin sulfate proteoglycans of the CNS glial scar. Mar 2003

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Characterization of antibody responses to endogenous and exogenous antigen in the nonobese diabetic mouse. Feb 2003

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Activation of phospholipase D1 by ADP-ribosylated RhoA. Feb 28 2003

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Leukotriene D(4) induces stress-fibre formation in intestinal epithelial cells via activation of RhoA and PKCdelta. Sep 1 2002

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Inhibito ry and stimulatory regulation of Rac and cell motility by the G12/13-Rho and Gi pathways integrated downstream of a single G protein-coupled sphingosine-1-phosphate receptor isoform. Mar 2003

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A regulated interaction of syntaxin 1A with the antidepressant-sensitive norepinephrine transporter establishes catecholamine clearance capacity. Mar 1 2003

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Tetanus toxin abolishes exocytosis of ROMK1 induced by inhibition of protein tyrosine kinase. 12 30 2002

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Plasma membrane targeting of SNAP-25 increases its local concentration and is necessary for SNARE complex formation and regulated exocytosis. Aug 15 2002

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Recombinant Lactobacillus johnsonii as a mucosal vaccine delivery vehicle. Jul 26 2002

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Sarcolipin overexpression in rat slow twitch muscle inhibits sarcoplasmic reticulum Ca2+ uptake and impairs contractile function. 09 16 2002

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Clostridium perfringens iota toxin. Mapping of the Ia domain involved in docking with Ib and cellular internalization. 09 06 2002

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Animal model of dementia induced by entorhinal synaptic damage and partial restoration of cognitive deficits by BDNF and carnitine. Nov 1 2002

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Hybrid tetanus toxin C fragment-diphtheria toxin translocation domain allows specific gene transfer into PC12 cells. Sep 2002

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EphA4 catalytic activity causes inhibition of RhoA GTPase in Xenopus laevis embryos. Mar 2002

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Reduced virus specific T helper cell induction by autologous dendritic cells in patients with chronic hepatitis B - restoration by exogenous interleukin-12. Oct 2002

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Critical components of a DNA fusion vaccine able to induce protective cytotoxic T cells against a single epitope of a tumor antigen. Oct 1 2002

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Insight into the potential for DNA idiotypic fusion vaccines designed for patients by analysing xenogeneic anti-idiotypic antibody responses. Sep 2002

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Humoral and cellular immune responses in mice immunized with recombinant Mycobacterium bovis Bacillus Calmette-Guerin producing a pertussis toxin- tetanus toxin hybrid protein. Oct 1999

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Galpha(13) stimulates Rho-dependent activation of the cyclooxygenase-2 promoter. Sep 24 1999

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Neosynthesis and activation of Rho by Escherichia coli cytotoxic necrotizing factor (CNF1) reverse cytopathic effects of ADP-ribosylated Rho. Sep 24 1999

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Relative contribution of endogenous neurotrophins in hippocampal long-term potentiation. Sep 15 1999

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Human dendritic cells very efficiently present a heterologous antigen expressed on the surface of recombinant gram-positive bacteria to CD4+ T lymphocytes. Sep 15 1999

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Antigenic variants in Bordetella pertussis strains isolated from vaccinated and unvaccinated children. Aug 1999

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Neuropil pattern formation and regulation of cell adhesion molecules in Drosophila optic lobe development depend on synaptobrevin. Sep 1 1999

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Cell surface-exposed tetanus toxin fragment C produced by recombinant Bacillus anthracis protects against tetanus toxin. Sep 1999

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The Src family tyrosine kinase is involved in Rho-dependent activation of c-Jun N-terminal kinase by Galpha12. Aug 5 1999

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Rho-kinase (ROK) promotes CD44v(3,8-10)-ankyrin interaction and tumor cell migration in metastatic breast cancer cells. 1999

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Rapid spine delivery and redistribution of AMPA receptors after synaptic NMDA receptor activation. Jun 11 1999

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Instruments for oral disease-intervention strategies: recombinant Lactobacillus casei expressing tetanus toxin fragment C for vaccination or myelin proteins for oral tolerance induction in multiple sclerosis. Apr 23 1999

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The IL-1 receptor and Rho directly associate to drive cell activation in inflammation. Jun 1999

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Enhancement of the endopeptidase activity of botulinum neurotoxin by its associated proteins and dithiothreitol. May 25 1999

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Immunogenicity of a Salmonella typhimurium aroA aroD vaccine expressing a nontoxic domain of Clostridium difficile toxin A. May 1999

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Activati on of protein kinase C by phorbol esters modulates alpha2beta1 integrin on MCF-7 breast cancer cells. Apr 10 1999

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Recom binant and truncated tetanus neurotoxin light chain: cloning, expression, purification, and proteolytic activity. Mar 1999

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Expression of disulphide-bridge-dependent conformational epitopes and immunogenicity of the carboxy-terminal 19 kDa domain of Plasmodium yoelii merozoite surface protein-1 in live attenuated Salmonella vaccine strains. Jan 1999

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Monitoring of scFv selected by phage display using detection of scFv-pIII fusion proteins in a microtiter scale assay. Nov 1 1998

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Lack of T-cell-mediated recognition of the fusion region of the pml/RAR-alpha hybrid protein by lymphocytes of acute promyelocytic leukemia patients. Mar 1996

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Conjugative transfer of the Escherichia coli-Clostridium perfringens shuttle vector pJIR1457 to Clostridium botulinum type A strains. Nov 1

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DNA vaccines with single-chain Fv fused to fragment C of tetanus toxin induce protective immunity against lymphoma and myeloma. Nov 199

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Production of an expression system for a synaptobrevin fragment to monitor cleavage by botulinum neurotoxin B. Jul 1998

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Ganglioside GT1b as a complementary receptor component for Clostridium botulinum neurotoxins. Aug 1998

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Localiz ation of RhoA GTPase to endothelial caveolae-enriched membrane domains. Jun 29 1998

20/6/55 11425098 98307523 PMID: 9645616
Soluble human lymphocyte activation gene-3 modulates allospecific T cell responses. May 1998

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MHC class II-associated invariant chain peptide replacement by T cell epitopes: engineered invariant chain as a vehicle for directed and enhanced MHC class II antigen processing and presentation. May 1998

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Expansion of autoreactive T cells in multiple sclerosis is independent of exogenous B7 costimulation. Feb 1 1998

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Rho-mediated contractility exposes a cryptic site in fibronectin and induces fibronectin matrix assembly. Apr 20 1998

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Associa tion of the myosin-binding subunit of myosin phosphatase and moesin: dual regulation of moesin phosphorylation by Rho-associated kinase and myosin phosphatase. Apr 20 1998

20/6/61 11308636 98187903 PMID: 9529054
The N-terminal part of the enzyme component (C2I) of the binary Clostridium botulinum C2 toxin interacts with the binding component 2II and functions as a carrier system for a Rho ADP-ribosylating C3-like fusion toxin. Apr 1998

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The small GTP-binding protein Rho1 is a multifunctional protein that regulates actin localization, cell polarity, and septum formation in the fission yeast Schizosaccharomyces pombe. Nov 1997

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Transient expression of botulinum neurotoxin C1 light chain differentially inhibits calcium and glucose induced insulin secretion in clonal beta-cells. Dec 8 1997

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Recombinant SNAP-25 is an effective substrate for Clostridium botulinum type A toxin endopeptidase activity in vitro. Oct 1997

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Identification of a recombinant synaptobrevin-thioredoxin fusion protein by capillary zone electrophoresis using laser-induced fluorescence detection. Jul 18 1997

20/6/67 11110175 97404407 PMID: 9256494
Construction of hybrid proteins that migrate retrogradely and transynaptically into the central nervous system. Aug 19 1997

20/6/68 11106181 97400359 PMID: 9257853
DNA vaccines against lymphoma: promotion of anti-idiotypic antibody responses induced by single chain Fv genes by fusion to tetanus toxin fragment C. Aug 15 1997

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Impaired class II expression and antigen uptake in monocytic cells after HIV-1 infection. Sep 1 1997

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Identification of a recombinant synaptobrevin-thioredoxin fusion protein by capillary zone electrophoresis using laser-induced fluorescence detection. Jul 18 1997

20/6/71 11050175 97404407 PMID: 9256494
Construction of hybrid proteins that migrate retrogradely and transynaptically into the central nervous system. Aug 19 1997

20/6/72 11046181 97400359 PMID: 9257853
DNA vaccines against lymphoma: promotion of anti-idiotypic antibody responses induced by single chain Fv genes by fusion to tetanus toxin fragment C. Aug 15 1997

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Heterologous expression of the cuticular-glutathione peroxidase of lymphatic filariae in an attenuated vaccine strain of Salmonella typhimurium abrogates H-2 restriction of specific antibody responses. Jun 1996

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Isolation of human anti-c-erbB-2 Fabs from a lymph node-derived phage display library. Jul 1997

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Rho proteins play a critical role in cell migration during the early phase of mucosal restitution. Jul 1 1997

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Cleavage of the synaptobrevin/vesicle-associated membrane protein (VAMP) of the mouse brain by the recombinant light chain of Clostridium botulinum type B toxin. May 15 1997

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Expres sion and immunogenicity of an Echinococcus granulosus fatty acid-binding protein in live attenuated Salmonella vaccine strains. Jun 1997

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Insulin-stimulated translocation of GLUT4 glucose transporters requires SNARE-complex proteins. Dec 24 1996

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Expression and immunogenicity of pertussis toxin S1 subunit- tetanus toxin fragment C fusions in Salmonella typhi vaccine strain CVD 908. Oct 1996

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Regulation mechanism of ERM (ezrin/radixin/moesin) protein/plasma membrane association: possible involvement of phosphatidylinositol turnover and Rho-dependent signaling pathway. Oct 1996

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A Salmonella typhimurium htrA live vaccine expressing multiple copies of a peptide comprising amino acids 8-23 of herpes simplex virus glycoprotein D as a genetic fusion to tetanus toxin fragment C protects mice from herpes simplex virus infection. Feb 1996

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Factors affecting the immunogenicity of tetanus toxin fragment C expressed in Lactococcus lactis. Jun 1996

20/6/84 10421671 96228050 PMID: 8647268
Botulinum neurotoxin light chains inhibit both Ca(2+)-induced and GTP analogue-induced catecholamine release from permeabilised adren chromaffin cells. May 20 1996

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Herpesvirus saimiri open reading frame 14, a protein encoded by T lymphotropic herpesvirus, binds to MHC class II molecules and stimulates T cell proliferation. May 1 1996

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Protein kinase A phosphorylation of RhoA mediates the morphological and functional effects of cyclic AMP in cytotoxic lymphocytes. Feb 1 19

20/6/87 10362180 96165391 PMID: 8571127
Identification of a putative target for Rho as the serine-threonine kinase protein kinase N. Feb 2 1996

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Expression of fragment C of tetanus toxin fused to a carboxyl-terminal fragment of diphtheria toxin in Salmonella typhi CVD 908 vaccine strain Nov 1995

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Expression of a large, nontoxic fragment of botulinum neurotoxin serotype A and its use as an immunogen. Oct 1995

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Detection of arginine-ADP-ribosylated protein using recombinant ADP-ribosylarginine hydrolase. Oct 10 1995

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Expression and purification of the light chain of botulinum neurotoxin A: a single mutation abolishes its cleavage of SNAP-25 and neurotoxic after reconstitution with the heavy chain. Nov 21 1995

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Production of antigen-specific human antibodies from mice engineered with human heavy and light chain YACs. Sep 29 1995

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Purification and assay of recombinant C3 transferase. 1995

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Amisyn, a novel syntaxin-binding protein that may regulate SNARE complex assembly. Aug 2 2002

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Calmodulin and lipid binding to synaptobrevin regulates calcium-dependent exocytosis. Aug 1 2002

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Trans-synaptic Eph receptor-ephrin signaling in hippocampal mossy fiber LTP. Jun 7 2002

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Vaccination with DNA encoding a single-chain TCR fusion protein induces anticlonotypic immunity and protects against T-cell lymphoma. Mar 2002

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The binary Clostridium botulinum C2 toxin as a protein delivery system: identification of the minimal protein region necessary for interaction toxin components. Feb 15 2002

20/6/100 09860389 21673341 PMID: 11814347
Structure-function analysis of the Rho-ADP-ribosylating exoenzyme C3stau2 from Staphylococcus aureus. Feb 5 2002

20/5/24 DIALOG(R)File 155:MEDLINE(R) (c) format only 2004 The Dialog Corp. All rts. reserv.
14124259 22316781 PMID: 12429212
Hybrid tetanus toxin C fragment-diphtheria toxin translocation domain allows specific gene transfer into PC12 cells.
Barati Shahram; Chegini Fariba; Hurtado Plinio; Rush Robert A; et al
Department of Human Physiology, Centre for Neuroscience, Flinders Medical Research Institute, Flinders University of South Australia, Adelaide, Australia. Shahram.Barati@post.flinders.edu.au
Experimental neurology (United States) Sep 2002, 177 (1) p75-87, ISSN 0014-4886 Journal Code: 0370712
Document type: Journal Article Languages: ENGLISH Main Citation Owner: NLM Record type: Completed Subfile: INDEX MEDICUS
To study the mechanism by which genes can efficiently be transferred into specific cell types, we have constructed several novel, single-chain multicomponent proteins by recombining the nontoxic C fragment of tetanus toxin and the translocation domain of diphtheria toxin together with the DNA-binding fragment of GAL4 transcription factor, for transportation of plasmid DNA into neuronal cells. The C fragment of tetanus toxin provided neuronal selectivity, the translocation domain of diphtheria toxin permitted endosomal escape, and the GAL4 domain provided binding to DNA. To assess the cellular tasks of each component in gene transfer, different combinations of these fragments were produced by polymerase chain reaction, expressed in Escherichia coli, and purified under native conditions from the soluble proteins. We show that only fusion proteins bearing the C fragment of tetanus toxin bind to gangliosides and, followed by their specific binding to differentiated PC12 cells, are internalized within 10 min. These proteins delivered the green fluorescence protein gene to PC12 cells, with the highest transfection efficiency achieved with proteins containing both the C fragment and the translocation domain. Addition of chloroquine elevated the transfection efficiency, which was further increased by incorporation of a nuclear localization signal in the delivery system. In addition, the effect of different DNA-condensing materials (poly-L-lysine, protamine, lysine(n=8)-trytophan(n=2)-lysine(n=8)) on gene transfer was investigated.
Tags: Animal; Support, Non-U.S. Gov't Descriptors: Diphtheria Toxin--genetics--GE; *Gene Transfer Techniques; *Peptide Fragments--genetics--GE; * Tetanus Toxin--genetics--GE; Amino Acid Sequence--genetics--GE; Binding Sites--genetics--GE; Cattle; Cell Line ; Diphtheria Toxin--metabolism--ME; Gene Transfer Techniques--trends--TD; Mice; Molecular Sequence Data; PC12 Cells; Peptide Fragments--metabolism --ME; Protein Transport--genetics--GE; Rats; Recombinant Fusion Proteins --genetics--GE; Recombinant Fusion Proteins --metabolism--ME; Saccharomyces cerevisiae Proteins--genetics--GE; Saccharomyces cerevisiae Proteins--metabolism--ME; Tetanus Toxin--metabolism--ME; Transcription Factors--genetics--GE; Transcription Factors--metabolism--ME CAS Registry No.: 0 (Diphtheria Toxin); 0 (GAL4 protein, S cerevisiae) ; 0 (Peptide Fragments); 0 (Recombinant Fusion Proteins); 0 (Saccharomyces cerevisiae Proteins); 0 (Tetanus Toxin); 0 (Transcription Factors); 0 (tetanus toxin fragment C)
Record Date Created: 20021113 Record Date Completed: 20021209

20/5/27 DIALOG(R)File 155:MEDLINE(R) (c) format only 2004 The Dialog Corp. All rts. reserv.
13963781 22229551 PMID: 12244189
Critical components of a DNA fusion vaccine able to induce protective cytotoxic T cells against a single epitope of a tumor antigen.
Rice Jason; Buchan Sarah; Stevenson Freda K; et al
Molecular Immunology Group, Tenovus Laboratory, Southampton University Hospitals Trust, Southampton, United Kingdom. j.rice@soton.ac.uk
Journal of immunology (Baltimore, Md. - 1950) (United States) Oct 1 2002, 169 (7) p3908-13, ISSN 0022-1767 Journal Code: 2985117R Document type: Journal Article Languages: ENGLISH Main Citation Owner: NLM Record type: Completed Subfile: AIM; INDEX MEDICUS
DNA vaccines can activate immunity against tumor Ags expressed as MHC class I-associated peptides. However, priming of CD8(+) CTL against weak tumor Ags may require adjuvant molecules. We have used a pathogen-derived sequence from tetanus toxin (fragment C (FrC)) fused to tumor Ag sequences to promote Ab and CD4(+) T cell responses. For induction of CD8(+) T cell responses, the FrC sequence has been engineered to remove potentially competitive MHC class I-binding epitopes and to improve presentation of tumor epitopes. The colon carcinoma CT26 expresses an endogenous retroviral gene product, gp70, containing a known H2-L(d)-restricted epitope (AH1). A DNA vaccine encoding gp70 alone was a poor inducer of CTL, and performance was not significantly improved by fusion of full-length FrC. However, use of a minimized domain of FrC, with the AH1 sequence fused to the 3' position, led to rapid induction of high levels of CTL. IFN-gamma-producing epitope-specific CTL were detectable ex vivo and these killed CT26 targets in vitro. The single epitope vaccine was more effective than GM-CSF-transfected CT26 tumor cells in inducing an AH1-specific CTL response and equally effective in providing protection against tumor challenge. Levels of AH1-specific CTL in vivo were increased following injection of tumor cells, and CTL expanded in vitro were able to kill CT26 cells in tumor bearers. Pre-existing immunity to tetanus toxoid had no effect on the induction of AH1-specific CTL. These data demonstrate the power of epitope-specific CTL against tumor cells and illustrate a strategy for priming immunity via a dual component DNA vaccine.
Tags: Animal; Support, Non-U.S. Gov't Descriptors: Antigens, Neoplasm--immunology--IM; *Cancer Vaccines --immunology--IM; *Cytotoxicity, Immunologic; *Epitopes, T-Lymphocyte --immunology--IM; *Lymphocyte Activation; * Recombinant Fusion Proteins --immunology--IM; *T-Lymphocytes, Cytotoxic--immunology--IM; *Vaccines, DNA --immunology--IM; Antigens, Neoplasm--administration and dosage--AD; Antigens, Neoplasm--genetics--GE; Cancer Vaccines --administration and dosage--AD; Cancer Vaccines--chemical synthesis--CS; Cancer Vaccines --genetics--GE; Colonic Neoplasms--immunology--IM; Colonic Neoplasms --pathology--PA; Colonic Neoplasms--prevention and control--PC; Cytotoxicity, Immunologic--genetics--GE; Epitopes, T-Lymphocyte --administration and dosage--AD; Epitopes, T-Lymphocyte--genetics--GE Growth Inhibitors--administration and dosage--AD; Growth Inhibitors --chemical synthesis--CS; Growth Inhibitors--genetics--GE; Growth Inhibitors--immunology--IM; Injections, Intramuscular; Interferon Type II --biosynthesis--BI; Lymphocyte Activation--genetics--GE; Mice; Mice, Inbred BALB C; Neoplasm Transplantation; Recombinant Fusion Proteins --administration and dosage--AD; Recombinant Fusion Proteins chemical synthesis--CS; Recombinant Fusion Proteins --genetics--GE; Retroviridae Proteins, Oncogenic--administration and dosage--AD; Retroviridae Proteins, Oncogenic--genetics--GE; Retroviridae Proteins, Oncogenic--immunology--IM; T-Lymphocytes, Cytotoxic--metabolism--M T-Lymphocytes, Cytotoxic --transplantation--TR; Tetanus Toxoid--administration and dosage--AD; Tetanus Toxoid--immunology--IM; Vaccin DNA--administration and dosage --AD; Vaccines, DNA--chemical synthesis--CS; Vaccines, DNA--genetics--GE; Viral Envelope Proteins--administration and dosage--AD; Viral Envelope Proteins--genetics--GE; Viral Envelope Proteins--immunology--IM CAS Registry No.: 0 (Antigens, Neoplasm); 0 (Cancer Vaccines); 0 (Epitopes, T-Lymphocyte); 0 (Growth Inhibitors); 0 (Recombinant Fusion Proteins); 0 (Retroviridae Proteins, Oncogenic); 0 (Tetanus Toxoid); 0 (Vaccines, DNA); 0 (Viral Envelope Proteins); 0 (glycoprotein gp70, leukemia viru envelope protein); 82115-62-6 (Interferon Type II)
Record Date Created: 20020923 Record Date Completed: 20021112

20/5/38 DIALOG(R)File 155:MEDLINE(R) (c) format only 2004 The Dialog Corp. All rts. reserv.
11925624 99369242 PMID: 10442633
The Src family tyrosine kinase is involved in Rho-dependent activation of c-Jun N-terminal kinase by Galpha12.
Nagao M; Kaziro Y; Itoh H
Faculty of Bioscience and Biotechnology, Tokyo Institute of Technology, Yokohama, Japan.
Oncogene (ENGLAND) Aug 5 1999, 18 (31) p4425-34, ISSN 0950-9232 Journal Code: 8711562
Document type: Journal Article Languages: ENGLISH Main Citation Owner: NLM Record type: Completed Subfile: INDEX MEDICUS
Gt12, a member of alpha subunit of heterotrimeric G protein G12 subfamily, has been shown to stimulate c-Jun N-terminal kinase (JNK) activity through the low molecular weight GTP-binding proteins Ras, Rac, and Cdc42. In this study using the transient expression of a constitutively activated mutant of Galpha12 (Galpha12Q229L) in human embryonic kidney (HEK) 293 cells, we found that Rho and Src family kinase are also involved in the Galpha12-induced activation of JNK. The activation of JNK by Galpha12Q229L was inhibited by dominant-negative RhoA(T19N), and botulinum C3 exoenzyme which specifically inactivates Rho. In addition, the expression of activated RhoA(G14V) elevated JNK activity in HEK 293 cells. The Galpha12Q229L-stimulated activation of JNK was blocked by a specific inhibitor of protein tyrosine kinases (PP2), and C-terminal Src kinase (Csk). Moreover, we observed that Galpha12Q229L stimulated Src family kinase activity and v-Src induce JNK activation. Interestingly, the v-Src-induced activation of JNK was inhibited by dominant-negative RhoA(T19N). In contrast Csk did not inhibit the JNK activation by activated RhoA(G14V). These results suggest that Rho and Src family kinase are required for the Galpha12-induced JNK activation, and that Src family kinase acts upstream of Rho activation in the JNK pathway.
Tags: Animal; Human; Support, Non-U.S. Gov't Descriptors: *Ca(2+)-Calmodulin Dependent Protein Kinase--metabolism--ME; *GTP-Binding Proteins--metabolism--ME; *Protein-Tyrosine Kinase--metabolism --ME; *Proto-Oncogene Proteins--metabolism--ME; 3T3 Cells; Amino Acid Substitution; COS Cells; Cell Line; DNA Primers; Enzyme Activation; GTP-Binding Proteins--genetics--GE; Mice; Mutagenesis, Site-Directed; Polymerase Chain Reaction; Proto-Oncogene Proteins--genetics--GE; Rats; Recombinant Fusion Proteins --metabolism--ME; Transfection; rhoA GTP-Binding Protein; src Homology Domains CAS Registry No.: 0 (DNA Primers); 0 (Gi2-alpha protein); 0 (Proto-Oncogene Proteins); 0 (Recombinant Fusion Proteins) Enzyme No.: EC 2.7.1.112 (Protein-Tyrosine Kinase); EC 2.7.1.123 (Ca(2+)-Calmodulin Dependent Protein Kinase); EC 2.7.10.- (c-Jun amino-terminal kinase); EC 3.6.1.- (GTP-Binding Proteins); EC 3.6.1.- (rhoA GTP-Binding Protein)
Record Date Created: 19990830 Record Date Completed: 19990830

20/7/51 DIALOG(R)File 155:MEDLINE(R) (c) format only 2004 The Dialog Corp. All rts. reserv.
11592988 99025406 PMID: 9809552
DNA vaccines with single-chain Fv fused to fragment C of tetanus toxin induce protective immunity against lymphoma and myeloma.
King C A; Spellerberg M B; Zhu D; Rice J; Sahota S S; Thompsett A R ; Hamblin T J; Radl J; Stevenson F K
Tenovus Laboratory, Southampton University Hospitals Trust, England.
Nature medicine (UNITED STATES) Nov 1998, 4 (11) p1281-6, ISSN 1078-8956 Journal Code: 9502015
Comment in Nat Med. 1998 Nov;4(11) 1239-40; Comment in PMID 9809542 Document type: Journal Article
Languages: ENGLISH Main Citation Owner: NLM Record type: Completed
Vaccination with idiotypic protein protects against B-cell lymphoma, mainly through anti-idiotypic antibody. For use in patients DNA vaccines containing single-chain Fv derived from tumor provide a convenient alternative vaccine delivery system. Howev single-chain Fv sequence alone induces low anti-idiotypic response and poor protection against lymphoma. Fusion of the gene encoding fragment C of tetanus toxin to single-chain Fv substantially promotes the anti-idiotypic response and induces strong protection against B-cell lymphoma. The same fusion design also induces protective immunity against a surface Ig-negative myeloma. These findings indicate that fusion to a pathogen sequence allows a tumor antigen to engage diverse immune mechanisms that suppress growth. This fusion design has the added advantage of overcoming potential tolerance to tumor th may exist in patients. Record Date Created: 19981130 Record Date Completed: 19981130

20/7/61 DIALOG(R)File 155:MEDLINE(R) (c) format only 2004 The Dialog Corp. All rts. reserv.
11308636 98187903 PMID: 9529054

The N-terminal part of the enzyme component (C2I) of the binary Clostridium botulinum C2 toxin interacts with the binding component C2II and functions as a carrier system for a Rho ADP-ribosylating C3-like fusion toxin.
Barth H; Hofmann F; Olenik C; Just I; Aktories K
Institut fur Pharmakologie und Toxikologie der Albert-Ludwigs-Universitat Freiburg, Germany.
Infection and immunity (UNITED STATES) Apr 1998, 66 (4) p1364-9, ISSN 0019-9567 Journal Code: 0246127
Document type: Journal Article Languages: ENGLISH Main Citation Owner: NLM Record type: Completed
The binary actin-ADP-ribosylating Clostridium botulinum C2 toxin consists of the enzyme component C2I and the binding component C2II, which are separate proteins. The active component C2I enters cells through C2II by receptor-mediated endocytosis and membrane translocation. The N-terminal part of C2I (C2IN), which consists of 225 amino acid residues but lacks ADP-ribosyltransferase activity, was identified as the C2II contact site. A fusion protein (C2IN-C3) of C2IN and the full-length C3-like ADP-ribosyltransferase from Clostridium limosum was constructed. The fusion protein C2IN-C3 ADP-ribosylated Rho but not actin in CHO cell lysates. Together with C2II, C2IN-C3 induced complete rounding up of CHO and HeLa cells after incubation for 3 h. No cell rounding was observed without C2II or with the original C3-like transferase from C. limosum. The data indicate that the N-terminal 225 amino acid residues of C2I are sufficient to cause the cellular uptake of C. limosum transferase via the binding component of C2II, thereby increasing the cytotoxicity of the C3-like exoenzyme several hundred-fold. Record Date Created: 19980409 Record Date Completed: 19980409

20/7/67 DIALOG(R)File 155:MEDLINE(R) (c) format only 2004 The Dialog Corp. All rts. reserv.
11110175 97404407 PMID: 9256494
Construction of hybrid proteins that migrate retrogradely and transynaptically into the central nervous system.
Coen L; Osta R; Maury M; Brulet P
Unite d'Embryologie Moleculaire, Unite de Recherche Associee 1947, Centre National de la Recherche Scientifique, Institut Pasteur, 25 rue du Dr. Roux, 75724 Paris Cedex 15, France.
Proceedings of the National Academy of Sciences of the United States of America (UNITED STATES) Aug 19 1997, 94 (17) p9400-5, ISSN 0027-8424 Journal Code: 7505876 Document type: Journal Article Languages: ENGLISH Main Citation Owner: NLM Record type: Completed
The nontoxic proteolytic C fragment of tetanus toxin (TTC peptide) has the same ability to bind nerve cells and be retrogradely transported through a synapse as the native toxin. We have investigated its potential use as an in vivo neurotropic carrier. In this work we show that a hybrid protein encoded by the lacZ-TTC gene fusion retains the biological functions of both proteins in vivo-i.e. , retrograde transynaptic transport of the TTC fragment and beta-galactosidase enzymatic activity. After intramuscular injection, enzymatic activity could be detected in motoneurons and connected neurons of the brainstem areas. This strategy could be used to deliver a biological activity to neurons from the periphery to the central nervous system. Such a hybrid protein could also be used to map synaptic connections between neural cells. Record Date Created: 19970917 Record Date Completed: 19970917

20/7/68 DIALOG(R)File 155:MEDLINE(R) (c) format only 2004 The Dialog Corp. All rts. reserv.
11106181 97400359 PMID: 9257853
DNA vaccines against lymphoma: promotion of anti-idiotypic antibody responses induced by single chain Fv genes by fusion to tetanus toxin fragment C.
Spellerberg M B; Zhu D; Thompsett A; King C A; Hamblin T J; Stevenson F K
Tenovus Laboratory, Southampton University Hospitals, United Kingdom.
Journal of immunology (Baltimore, Md. - 1950) (UNITED STATES) Aug 15 1997, 159 (4) p1885-92, ISSN 0022-1767 Journal Code: 2985117R Document type: Journal Article Languages: ENGLISH Main Citation Owner: NLM Record type: Completed
Idiotypic determinants can act as tumor-associated Ags for B cell lymphoma. Vaccination with idiotypic protein and adjuvant is known to induce specific protection against lymphoma challenge in mice, largely mediated by anti-idiotypic Ab. For facilitating the approach for patients, the V(H) and V(L) genes used to encode the individual idiotypic determinants of each tumor can be obtained by PCR and assembled as single chain Fv (scFv). DNA vaccines containing scFv sequences alone induce low and poorly reproducible levels of anti-idiotypic Ab, likely to be insufficient to suppress tumor in patients. In addition, it may be necessary to break tolerance to Id in tumor bearers. By fusing the gene for fragment C of tetanus toxin to the C terminus of human scFv, we have promoted the anti-scFv Ab response in mice by >50-fold in three of three cases. The induced Abs are mainly against idiotypic determinants, and react specifically with patients' tumor cells, indicating optimal folding of the scFv molecule in the fusion protein. For both antigenic components of the DNA vaccine, the IgG subclass distribution showed a relative increase in IgG2a as compared with vaccination with IgM protein in adjuvant. In patients, the fusion gene should both promote anti-idiotypic Ab and induce Abs against fragment C of tetanus toxin. The latter response would provide a potentially useful comparative measure of the ability of patients to respond to conventional Ag delivered via DNA. Record Date Created: 19970828 Record Date Completed: 19970828

20/7/71 DIALOG(R)File 155:MEDLINE(R) (c) format only 2004 The Dialog Corp. All rts. reserv.
11050175 97404407 PMID: 9256494
Construction of hybrid proteins that migrate retrogradely and transynaptically into the central nervous system.
Coen L; Osta R; Maury M; Brulet P
Unite d'Embryologie Moleculaire, Unite de Recherche Associee 1947, Centre National de la Recherche Scientifique, Institut Pasteur, 25 rue du Dr. Roux, 75724 Paris Cedex 15, France.
Proceedings of the National Academy of Sciences of the United States of America (UNITED STATES) Aug 19 1997, 94 (1 p9400-5, ISSN 0027-8424 Journal Code: 7505876 Document type: Journal Article Languages: ENGLISH Main Citation Owner: NLM Record type: Completed
The nontoxic proteolytic C fragment of tetanus toxin (TTC peptide) has the same ability to bind nerve cells and be retrogradel transported through a synapse as the native toxin. We have investigated its potential use as an in vivo neurotropic carrier. In t work we show that a hybrid protein encoded by the lacZ-TTC gene fusion retains the biological functions of both proteins in viv i.e. , retrograde transynaptic transport of the TTC fragment and beta-galactosidase enzymatic activity. After intramuscular injection, enzymatic activity could be detected in motoneurons and connected neurons of the brainstem areas. This strategy could be used to deliver a biological activity to neurons from the periphery to the central nervous system. Such a hybrid protein could also be used to map synaptic connections between neural cells. Record Date Created: 19970917 Record Date Complet 19970917

20/7/76 DIALOG(R)File 155:MEDLINE(R) (c) format only 2004 The Dialog Corp. All rts. reserv.
10961209 97313862 PMID: 9170263
Cleavage of the synaptobrevin/vesicle-associated membrane protein (VAMP) of the mouse brain by the recombinant light chain of Clostridium botulinum type B toxin.
Rhee S D; Jung H H; Yang G H; Moon Y S; Yang K H
Department of Biological Sciences, Korea Advanced Institute of Science and Technology, Taejon, South Korea.
FEMS microbiology letters (NETHERLANDS) May 15 1997, 150 (2) p203-8, ISSN 0378-1097 Journal Code: 7705721
Document type: Journal Article Languages: ENGLISH Main Citation Owner: NLM Record type: Completed
The light chain of Clostridium botulinum type B toxin was expressed in Escherichia coli using the expression vector pEt-3a containing phage T7 promoter. The expressed protein was then purified by DEAE-cellulose and phosphocellulose chromatography and the proteolytic activity of the purified light chain was studied. The purified recombinant light chain cleaved synaptobrevin when mixed with the mouse brain microsome and the proteolytic activity of the light chain was inhibited if a met chelating agent such as EDTA or 2,2'-dipyridyl was added. The recombinant light chain cleaved synaptobrevin more effectivel than the native type B toxin. When the native toxin was trypinized and was reduced with DTT, its proteolytic activity was simila to that of the recombinant light chain. Record Date Created: 19970714 Record Date Completed: 19970714

20/7/88 DIALOG(R)File 155:MEDLINE(R) (c) format only 2004 The Dialog Corp. All rts. reserv.
10361266 96164477 PMID: 8578848
Expression of fragment C of tetanus toxin fused to a carboxyl-terminal fragment of diphtheria toxin in Salmonella typhi CVD 908 vaccine strain.
Gomez-Duarte O G; Galen J; Chatfield S N; Rappuoli R; Eidels L; Levine M M
Department of Medicine, University of Maryland School of Medicine, Baltimore 21201, USA.
Vaccine (ENGLAND) Nov 1995, 13 (16) p1596-602, ISSN 0264-410X Journal Code: 8406899 Contract/Grant No.: NO1 AI15096; AI; NIAID; NO1 AI45251; AI; NIAID; RO1 A129471; PHS Document type: Journal Article Languages: ENGLISH Main Citation Owner: NLM Record type: Completed
We report the expression of fragment C of tetanus toxin (FC) fused to the eukaryotic cell binding domain (the carboxyl-termin of diphtheria toxin (FC-bDt fusion) in attenuated Salmonella typhi live vector vaccine strain CVD 908. The FC-bDt protein fusio was constructed using plasmid pTETnir15 which carries the gene encoding FC under control of the nirB promoter (nirBP). The open reading frame for FC was modified to incorporate an in-frame glycine-proline hinge region and a set of four restriction sit at the 3' end of the FC gene. A 482 bp DNA fragment encoding the eukaryotic cell binding domain of diphtheria toxin was then inserted at the 3' end of the modified FC gene to create an in-frame FC-bDt fusion gene. The resulting plasmid, pOG215, was able to express the FC-bDt fusion protein in both Escherichia coli DH5a and S. typhi CVD 908, as evidenced by Western immunoblots using anti-FC and anti-C-terminal diphtheria toxin monoclonal antibodies. Maximum expression of the FC-bDt fusion protein was achieved by growing CVD 908(pOG215) at the low oxidation-reduction potential of thioglycollate broth, i.e. conditions that activate nirBP and drive transcription of the FC-bDt fusion gene. Whereas maximum expression of FC alone w also observed using thioglycollate broth, expression of bDt alone was unsuccessful using a variety of growth conditions. FC fusions constitute one strategy to "rescue" expression of proteins which are otherwise difficult to express. Record Date Create 19960312 Record Date Completed: 19960312

20/7/82 DIALOG(R)File 155:MEDLINE(R) (c) format only 2004 The Dialog Corp. All rts. reserv.
10600306 96417858 PMID: 8820649
A Salmonella typhimurium htrA live vaccine expressing multiple copies of a peptide comprising amino acids 8-23 of herpes simplex virus glycoprotein D as a genetic fusion to tetanus toxin fragment C protects mice from herpes simplex virus infection.
Chabalgoity J A; Khan C M; Nash A A; Hormaeche C E
Department of Microbiology, University of Newcastle, Newcastle upon Tyne, UK.
Molecular microbiology (ENGLAND) Feb 1996, 19 (4) p791-801, ISSN 0950-382X Journal Code: 8712028 Document type: Journal Article Languages: ENGLISH Main Citation Owner: NLM Record type: Completed

Multiple tandem copies of an immunogenic epitope comprising amino acids 8-23 of glycoprotein D of herpes simplex virus (HSV) were expressed as C-terminal fusions to tetanus toxin fragment C (TetC) in different Salmonella typhimurium live vaccine strains. Expression of the longer fusions was best in strains harbouring a lesion in htrA, a stress protein gene. SL3261, an aroA strain, did not effectively express the longer fusions. Mice immunised with an S. typhimurium C5 htrA mutant expressing fusions with two or four copies of the peptide made an antibody response to both the peptide and TetC, whereas constructs expressing one copy of the peptide only elicited antibody to TetC. A non-immunogenic octameric fusion underwent rearrangements in vivo resulting in a predominantly monomeric fusion. In contrast, the S. typhimurium SL3261 aroA vaccine expressing the TetC-tetrameric fusion did not elicit antibody to the peptide. Sera from mice immunised with a single dose of the dimer and tetramer fusions in the htrA strain neutralised HSV in vitro, and the mice were protected from HSV infection as measured by a reduction in virus load in the ear pinna. We have previously shown that mice vaccinated with salmonella expressing TetC are protected against tetanus toxin and virulent salmonella challenge. These results suggest that it may be possible to develop a multivalent vaccine against salmonellosis, tetanus and HSV. Record Date Created: 19961216 Record Date Completed: 19961216

20/7/88 DIALOG(R)File 155:MEDLINE(R) (c) format only 2004 The Dialog Corp. All rts. reserv.
10361266 96164477 PMID: 8578848
Expression of fragment C of tetanus toxin fused to a carboxyl-terminal fragment of diphtheria toxin in Salmonella typhi CVD 908 vaccine strain.
Gomez-Duarte O G; Galen J; Chatfield S N; Rappuoli R; Eidels L; Levine M M
Department of Medicine, University of Maryland School of Medicine, Baltimore 21201, USA.
Vaccine (ENGLAND) Nov 1995, 13 (16) p1596-602, ISSN 0264-410X Journal Code: 8406899
Contract/Grant No.: NO1 AI15096; AI; NIAID; NO1 AI45251; AI; NIAID; RO1 A129471; PHS Document type: Journal Article
Languages: ENGLISH Main Citation Owner: NLM Record type: Completed
We report the expression of fragment C of tetanus toxin (FC) fused to the eukaryotic cell binding domain (the carboxyl-terminus) of diphtheria toxin (FC-bDt fusion) in attenuated Salmonella typhi live vector vaccine strain CVD 908. The FC-bDt protein fusion was constructed using plasmid pTETnir15 which carries the gene encoding FC under control of the nirB promoter (nirBP). The open reading frame for FC was modified to incorporate an in-frame glycine-proline hinge region and a set of four restriction sites at the 3' end of the FC gene. A 482 bp DNA fragment encoding the eukaryotic cell binding domain of diphtheria toxin was then inserted at the 3' end of the modified FC gene to create an in-frame FC-bDt fusion gene. The resulting plasmid, pOG215, was able to express the FC-bDt fusion protein in both Escherichia coli DH5a and S. typhi CVD 908, as evidenced by Western immunoblots using anti-FC and anti-C-terminal diphtheria toxin monoclonal antibodies. Maximum expression of the FC-bDt fusion protein was achieved by growing CVD 908(pOG215) at the low oxidation-reduction potential of thioglycollate broth, i.e. in conditions that activate nirBP and drive transcription of the FC-bDt fusion gene. Whereas maximum expression of FC alone was also observed using thioglycollate broth, expression of bDt alone was unsuccessful using a variety of growth conditions. FC fusions constitute one strategy to "rescue" expression of proteins which are otherwise difficult to express. Record Date Created: 19960312 Record Date Completed: 19960312

20/7/89 DIALOG(R)File 155:MEDLINE(R) (c) format only 2004 The Dialog Corp. All rts. reserv.
10348836 96151333 PMID: 8599190
Expression of a large, nontoxic fragment of botulinum neurotoxin serotype A and its use as an immunogen.
LaPenotiere H F; Clayton M A; Middlebrook J L
Toxinology Division, U.S. Army Medical Research Institute of Infectious Diseases, Frederick, MD 21702-5011, USA.
Toxicon - official journal of the International Society on Toxinology (ENGLAND) Oct 1995, 33 (10) p1383-6, ISSN 0041-0101 Journal Code: 1307333 Document type: Journal Article; Review; Review, Tutorial Languages: ENGLISH
Main Citation Owner: NLM Record type: Completed
Using the polymerase chain reaction, a large fragment of botulinum toxin was placed in two expression systems, one designed to produce a fusion protein product and another designed to produce only the toxin fragment. Expression of the fragment in the latter system was inconsistent. Expression of the fusion protein was easily measurable by ELISA. Mice were vaccinated with crude fusion protein, then challenged with native toxin. Mice receiving two immunizations were partially protected from up to 1200 LD50, suggesting that this toxin fragment may be a good vaccine candidate to replace the currently used toxoid. (8 Refs.) Record Date Created: 19960419 Record Date Completed: 19960419

20/7/99 DIALOG(R)File 155:MEDLINE(R) (c) format only 2004 The Dialog Corp. All rts. reserv.
09916932 21826459 PMID: 11741886
The binary Clostridium botulinum C2 toxin as a protein delivery system: identification of the minimal protein region necessary for interaction of toxin components.
Barth Holger; Roebling Robert; Fritz Michaela; Aktories Klaus
Institut fur Experimentelle und Klinische Pharmakologie und Toxikologie der Albert-Ludwigs-Universitat Freiburg, Albertstrasse 25, D-79104 Freiburg Germany. barthh@uni-freiburg.de
Journal of biological chemistry (United States) Feb 15 2002, 277 (7) p5074-81, ISSN 0021-9258 Journal Code: 2985121R
Document type: Journal Article Languages: ENGLISH Main Citation Owner: NLM Record type: Completed
The binary Clostridium botulinum C2 toxin is composed of the enzyme component C2I and the binding component C2II, which are individual and non-linked proteins. Activated C2IIa mediates cell binding and translocation of C2I into the cytoplasm. C2I ADP-ribosylates G-actin at Arg-177 to depolymerize actin filaments. A fusion toxin containing the N-terminal domain of C2I (residues 1-225) transports C3 ADP-ribosyltransferase from Clostridium limosum into cells (Barth, H., Hofmann, F., Olenik, C. Just, I., and Aktories, K. (1998) Infect. Immun. 66, 1364-1369). We characterized the adaptor function of C2I and its interaction with C2IIa. The fusion toxin GST-C2I(1-225)-C3 was efficiently transported by C2IIa, indicating that C2IIa translocates proteins into the cytosol even when the C2I(1-225) adaptor was positioned in the middle of a fusion protein. Amino acid residues 1-87 o C2I were sufficient for interaction with C2IIa and for translocation of C2I fusion toxins into HeLa cells. Residues 1-87 were the minimal part of C2I to bind to C2IIa on the cell surface, as detected by fluorescence-activated cytometry. An excess of C2I(1-8 (but not of further truncated C2I fragments) competed with Alexa488-labeled C2I for binding to C2IIa. Also, the fragment C2I(3 431) and the fusion toxin C2I(30-225)-C3 competed with C2I-Alexa488 for binding to C2IIa. C2I(30-225)-C3 did not induce cytotoxic effects on cells when applied together with C2IIa, indicating that amino acid residues 1-29 are involved in translocatio of C2I but are not absolutely essential for binding to C2IIa. Record Date Created: 20020211 Record Date Completed: 2002032

21/6/1 14464053 22127360 PMID: 12126902
Recombinant Lactobacillus johnsonii as a mucosal vaccine delivery vehicle. Jul 26 2002

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Recombinant SNAP-25 is an effective substrate for Clostridium botulinum type A toxin endopeptidase activity in vitro. Oct 1997

21/6/3 10600306 96417858 PMID: 8820649
A Salmonella typhimurium htrA live vaccine expressing multiple copies of a peptide comprising amino acids 8-23 of herpes simplex virus glycoprotein D as a genetic fusion to tetanus toxin fragment C protects mice from herpes simplex virus infection. Feb 1996

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Expression and purification of the light chain of botulinum neurotoxin A: a single mutation abolishes its cleavage of SNAP-25 and neurotoxic after reconstitution with the heavy chain. Nov 21 1995

21/6/5 08198098 94264020 PMID: 7911329
A single mutation in the recombinant light chain of tetanus toxin abolishes its proteolytic activity and removes the toxicity seen after reconstitution with native heavy chain. Jun 7 1994

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New strategies for vaccination and imunomodulation in NHL. 2001

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DNA fusion vaccines against B-cell tumors. Dec 2001

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Surface display of recombinant proteins on Bacillus subtilis spores. Nov 2001

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Plant viral genes in DNA idiotypic vaccines activate linked CD4+ T-cell mediated immunity against B-cell malignancies. Aug 2001

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DNA fusion vaccine designed to induce cytotoxic T cell responses against defined peptide motifs: implications for cancer vaccines. Aug 1 2001

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Lactic acid bacteria as live vaccines. Jan 2000

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Antibodies with infinite affinity. Jul 17 2001

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Conditional restoration of hippocampal synaptic potentiation in Glur-A-deficient mice. Jun 29 2001

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Human urotensin II-induced contraction and arterial smooth muscle cell proliferation are mediated by RhoA and Rho-kinase. Jun 8 2001

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A common exocytotic mechanism mediates axonal and dendritic outgrowth. Jun 1 2001

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Neuronal targeting of cardiotrophin-1 by coupling with tetanus toxin C fragment. May 2001

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Heterologous gene expression in bacterial systems under reduced oxygen tensions. Small-scale optimization precedes industrial fermentation. Feb 2001

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Sup35p yeast prion-like protein as an adapter for production of the Gag-p55 antigen of HIV-1 and the L-chain of botulinum neurotoxin in Saccharomyces cerevisiae. Jan-Feb 2001

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Recombinant vaccines against infectious hematopoietic necrosis virus: production by the Caulobacter crescentus S-layer protein secretion system and evaluation in laboratory trials. Jan 26 2001

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Genetically altered AMPA-type glutamate receptor kinetics in interneurons disrupt long-range synchrony of gamma oscillation. Mar 13 2001

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Low concentrations of lipopolysaccharide synergize with peptides to augment human T-cell proliferation and can prevent the induction of non-responsiveness by CTLA4-Ig. Jan 2001

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Rho GTPases: secretion and actin dynamics in permeabilized mast cells. 2000

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Membrane localization and biological activity of SNAP-25 cysteine mutants in insulin-secreting cells. Sep 2000

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Cloning, expression, and one-step purification of the minimal essential domain of the light chain of botulinum neurotoxin type A. Jun 2000

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Enhancement of diphtheria toxin potency by replacement of the receptor binding domain with tetanus toxin C-fragment: a potential vector for delivering heterologous proteins to neurons. Jun 2000

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Characterization of human inducible costimulator ligand expression and function. May 1 2000

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Ephrin-A5 induces collapse of growth cones by activating Rho and Rho kinase. Apr 17 2000

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Tetanus toxin fragment C expressed in live Salmonella vaccines enhances antibody responses to its fusion partner Schistosoma haematobium glutathione S-transferase. May 2000

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High-level expression of tetanus toxin fragment C-thioredoxin fusion protein in Escherichia coli. Apr 2000

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Flow cytometric measurement of intracellular cytokines detects immune responses in MUC1 immunotherapy. Mar 2000

20/6/138 08914955 20202758 PMID: 10736202
Ectopic expression of NCAM in skeletal muscle of transgenic mice results in terminal sprouting at the neuromuscular junction and altered structure but not function. Mar 2000

20/6/139 08912838 20200471 PMID: 10734125
Rho family proteins modulate rapid apoptosis induced by cytotoxic T lymphocytes and Fas. Mar 31 2000

20/6/140 08900494 20187498 PMID: 10722622
Immunogenicity and efficacy in aotus monkeys of four recombinant Plasmodium falciparum vaccines in multiple adjuvant formulations based on the 19-kilodalton C terminus of merozoite surface protein 1. Apr 2000

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Identification and characterization of functional subunits of Clostridium botulinum type A progenitor toxin involved in binding to intestinal microvilli and erythrocytes. Feb 11 2000

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Botulinum neurotoxin E-insensitive mutants of SNAP-25 fail to bind VAMP but support exocytosis. Dec 1999

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Generation of an expression library in the baculovirus expression vector system. Jun 1995

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Characterization of recombinant tetanus toxin derivatives suitable for vaccine development. Aug 1995

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Construction, expression, and immunogenicity of multiple tandem copies of the Schistosoma mansoni peptide 115-131 of the P28 glutathi S-transferase expressed as C-terminal fusions to tetanus toxin fragment C in a live aro-attenuated vaccine strain of Salmonella. Dec 15 1994

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Probing the action of Clostridium difficile toxin B in Xenopus laevisoocytes. Jun 1994

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Antigen-specific human monoclonal antibodies from mice engineered with human Ig heavy and light chain YACs. May 1994

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A post-docking role for synaptobrevin in synaptic vesicle fusion. Jun 1994

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A single mutation in the recombinant light chain of tetanus toxin abolishes its proteolytic activity and removes the toxicity seen after reconstitution with native heavy chain. Jun 7 1994

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Assays for adjuvanticity of new formulations and of carrier proteins for inducing antibody responses to selected immunogens in the squirrel monkey Saimiri sciureus. Apr 1994

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Neutralizing antibodies and immunoprotection against pertussis and tetanus obtained by use of a recombinant pertussis toxin- tetanus toxin fusion protein. Feb 1994

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Comparison of the effects of adjuvants and adjuvant doses on the quantitative and qualitative antibody response to selected antigens in New World squirrel monkeys Saimiri sciureus. 1993

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Specific interaction of lymphocyte function-associated antigen 3 with CD2 can inhibit T cell responses. Jul 1 1993

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Recombinant human antibodies: linkage of an Fab fragment from a combinatorial library to an Fc fragment for expression in mammalian cell culture. Apr 1993

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A bacteriophage lambda vector for the cloning and expression of immunoglobulin Fab fragments on the surface of filamentous phage. Jun 15 1993

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Therapeutic human antibodies derived from PCR amplification of B-cell variable regions. Dec 1992

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Cloning of a Clostridium botulinum type B toxin gene fragment encoding the N-terminus of the heavy chain. Feb 1 1992

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Effects of a soluble CD4 and CD4-Pseudomonas exotoxin A chimeric protein on human peripheral blood lymphocytes: lymphocyte activation and anti-HIV activity in vitro. Oct 1991

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Assembly of combinatorial antibody libraries on phage surfaces: the gene III site. Sep 15 1991

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Charact erization of the C3 gene of Clostridium botulinum types C and Dand its expression in Escherichia coli. Oct 1991

20/6/177 06865780 91105879 PMID: 1988163
Inhibition of human antigen-specific memory B cell response in vitro by a diphtheria toxin-related interleukin 2 fusion protein. Feb 1991

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Expression of tetanus toxin subfragments in vitro and characterization of epitopes. Nov 1989

20/7/136 DIALOG(R)File 155:MEDLINE(R) (c) format only 2004 The Dialog Corp. All rts. reserv.
08922959 20211255 PMID: 10744952
High-level expression of tetanus toxin fragment C-thioredoxin fusion protein in Escherichia coli.
Ribas A V; Ho P L; Tanizaki M M; Raw I; Nascimento A L
Center of Biotechnology, Instituto Butantan, Av. Vital Brasil, 1500, CEP 05503-900, Sao Paulo, SP, Brazil.
Biotechnology and applied biochemistry (ENGLAND) Apr 2000, 31 (Pt 2) p91-4, ISSN 0885-4513 Journal Code: 860946
Document type: Journal Article Languages: ENGLISH Main Citation Owner: NLM Record type: Completed
An insert of Clostridium tetani DNA corresponding to fragment C of tetanus toxin was amplified by PCR. This 1.4 kb fragment was cloned into the high-expression vector pET32a, under control of the T7 promoter. Expression of this plasmid in Escherich coli BL21(DE3) resulted in the production of a fusion protein (approximately 62 kDa) consisting of 112 amino acids of thioredo and approximately 450 amino acids of fragment C. This fusion protein was recognized by anti- tetanus toxoid antiserum in an ELISA and on immunoblots. The recombinant fragment-C-thioredoxin protein was purified significantly in one step by Ni(2+)-chelate Sepharose, the final yield being approximately 35 mg/l. Immunization of animals with the recombinant protein produce antibodies that were able to recognize the tetanus toxin. By using this gene-fusion expression system we produced soluble fragment C of tetanus toxin in a high yield, preventing many problems inherent in the use of other expression systems that produce either insoluble fragment C in inclusion bodies, or a soluble form, but in low yield, using E. coli as the expression host Record Date Created: 20000525 Record Date Completed: 20000525

20/7/132 DIALOG(R)File 155:MEDLINE(R) (c) format only 2004 The Dialog Corp. All rts. reserv.
08990056 20281858 PMID: 10820215
Enhancement of diphtheria toxin potency by replacement of the receptor binding domain with tetanus toxin C-fragment: potential vector for delivering heterologous proteins to neurons.
Francis J W; Brown R H; Figueiredo D; Remington M P; Castillo O; Schwarzschild M A; Fishman P S; Murphy J R; vanderSpek J C
Cecil B. Day Center for Neuromuscular Research, Department of Neurology, Massachusetts General Hospital and Harvard Medical School, Charlestown, MA 02129, USA. francis@helix.mgh.harvard.edu
Journal of neurochemistry (UNITED STATES) Jun 2000, 74 (6) p2528-36, ISSN 0022-3042 Journal Code: 2985190R
Contract/Grant No.: 1P01NS31248-02; NS; NINDS; 5F32HS10064; HS; AHCPR; R01 NS38679-01; NS; NINDS
Document type: Journal Article Languages: ENGLISH Main Citation Owner: NLM Record type: Completed
This study describes the expression, purification, and characterization of a recombinant fusion toxin, DAB(389)TTC, compose of the catalytic and membrane translocation domains of diphtheria toxin (DAB(389)) linked to the receptor binding fragment of tetanus toxin (C-fragment). As determined by its ability to inhibit cellular protein synthesis in primary neuron cultures, DAB(389)TTC was approximately 1,000-fold more cytotoxic than native diphtheria toxin or the previously described fusion toxi DAB(389)MSH. The cytotoxic effect of DAB(389)TTC on cultured cells was specific toward neuronal-type cells and was blocke by coincubation of the chimeric toxin with tetanus antitoxin. The toxicity of DAB(389)TTC, like that of diphtheria toxin, was dependent on passage through an acidic compartment and ADP-ribosyltransferase activity of the DAB(389) catalytic fragment These results suggest that a catalytically inactive form of DAB(389)TTC may be useful as a nonviral vehicle to deliver exogeno proteins to the cytosolic compartment of neurons. Record Date Created: 20000602 Record Date Completed: 20000602

20/7/114 DIALOG(R)File 155:MEDLINE(R) (c) format only 2004 The Dialog Corp. All rts. reserv.
09481983 21258150 PMID: 11358482
Neuronal targeting of cardiotrophin-1 by coupling with tetanus toxin C fragment.
Bordet T; Castelnau-Ptakhine L; Fauchereau F; Friocourt G; Kahn A; Haase G
INSERM U.129, Institut Cochin de Genetique Moleculaire, 24, Rue du Faubourg St Jacques, 75014 Paris, France.
Molecular and cellular neurosciences (United States) May 2001, 17 (5) p842-54, ISSN 1044-7431 Journal Code: 910009
Document type: Journal Article Languages: ENGLISH Main Citation Owner: NLM Record type: Completed
Cardiotrophin-1 (CT-1) is a potent neurotrophic factor for motoneurons but its clinical use in motor neuron diseases is preclud by side effects on the heart and liver. We explored the possibility of targeting CT-1 to neurons by coupling with the tetanus tox fragment TTC. Genetic fusion proteins between CT-1 or GFP and TTC were produced in Escherichia coli and assayed in vitro contrast to uncoupled CT-1 or GFP, TTC-coupled proteins bound with high affinity to cerebral neurons and spinal cord motoneurons and were rapidly internalized. Glia, hepatocytes, or cardiomyocytes did not show detectable binding or uptake of TTC-coupled proteins. Similar to CT-1, TTC-coupled CT-1 induced IL-6 secretion by KB cells, activated Reg-2 gene expressio and promoted motoneuron survival in a dose-dependent manner. In vivo studies will test whether TTC-coupled CT-1 might be targeted to degenerating spinal cord or brain-stem motoneurons and migrate trans-synaptically to cortical motoneurons, which are also affected in amyotrophic lateral sclerosis. Copyright 2001 Academic Press. Record Date Created: 20010518 Record Date Completed: 20010809
Tags: Animal; Human; Support, Non-U.S. Gov't Descriptors: Cells, Cultured--drug effects--DE; *Cytokines--pharmacology --PD; *Motor Neuro Disease--drug therapy--DT; *Motor Neurons--drug effects --DE; *Nerve Growth Factors--pharmacology--PD; *Peptide Fragments --pharmacology--PD; * Recombinant Fusion Proteins --pharmacology--PD; * Tetanus Toxin--pharmacology--PD; Brain--cytology--CY; Brain -

drug effects--DE; Brain--metabolism--ME; Cell Survival--drug effects--DE; Cell Survival--physiology--PH; Cells, Cultured--cytology--CY; Cells, Cultured --metabolism--ME; Cytokines--genetics--GE; Dose-Response Relationship, Drug ; Escherichia coli--genetics--GE; Fetus; Gene Expression--drug effects--DE; Gene Expression--physiology--PH; Heart--drug effects--DE; Heart --physiology--PH; Hepatocytes--cytology--CY; Hepatocytes--drug effects--DE ; Hepatocytes--metabolism--ME; Interleukin-6--genetics--GE; Interleukin-6 --metabolism--ME; Interleukin-6--secretion--SE; Luminescent Proteins --analysis--AN; Luminescent Proteins--genetics--GE; Mice; Motor Neuron Disease--metabolism--ME; Motor Neuron Disease--physiopathology--PP; Motor Neurons--cytology--CY; Motor Neurons--metabolism--ME; Nerve Growth Factors --genetics--GE; Peptide Fragments--genetics--GE; Protein Engineering --methods--MT; Recombinant Fusion Proteins --chemical synthesis--CS; Recombinant Fusion Proteins --genetics--GE; Signal Transduction--drug effects--DE; Signal Transduction--genetics--GE; Spinal Cord--cytology--CY; Spinal Cord--drug effects--DE; Spinal Cord--metabolism--ME; Tetanus Toxin--genetics--GE CAS Registry No.: 0 (Cytokines); 0 (Interleukin-6); 0 (Luminescent Proteins); 0 (Nerve Growth Factors); 0 (Peptide Fragments); 0 (Recombinant Fusion Proteins); 0 (Tetanus Toxin); 0 (cardiotrophin 1); 0 (tetanus toxin fragment C); 147336-22-9 (green fluorescent protein)

20/7/151 DIALOG(R)File 155:MEDLINE(R) (c) format only 2004 The Dialog Corp. All rts. reserv.
08548161 95236461 PMID: 7720079
Utilization of soluble fusion proteins for induction of T cell proliferation.
Kirschmann D A; De Ciechi P A; Bono C P; Zacheis M L; Schwartz B D; Woulfe S L
Department of Immunology and Glycobiology, Monsanto Corporate Research/G. D. Searle, St. Louis, Missouri 63198, USA.
Cellular immunology (UNITED STATES) Feb 1995, 160 (2) p193-8, ISSN 0008-8749 Journal Code: 1246405
Document type: Journal Article Languages: ENGLISH Main Citation Owner: NLM Record type: Completed
A peptide display library was evaluated as a means to identify peptide binding motifs for class II molecules. Peptides expressed as part of a soluble fusion protein with a maltose binding protein (malE) were produced by Escherichia coli. Constructs containing the high-affinity binding influenza hemagglutinin peptide 307W-319 (mal-HA) or the low-affinity binding tetanus toxoid peptide 830-843 (mal-TT) were used as controls. mal-HA, but not mal-TT, inhibited synthetic biotinylated-HA peptide from binding to purified DR4 Dw4 molecules in a dose-dependent manner. The fusion-peptide presentation system was also evaluated for its ability to induce antigen-specific T cell proliferation. DR4 Dw4+ B cells pulsed with mal-HA, but not mal-TT, induced dose-dependent proliferation of an HA-specific DR4 Dw4-restricted T cell line to the same extent as synthetic HA peptide. Using this type of peptide display library, it may be possible to determine the antigenic specificity of T cell clones isolated from patients with autoimmune diseases. Record Date Created: 19950522 Record Date Completed: 19950522

20/7/164 DIALOG(R)File 155:MEDLINE(R) (c) format only 2004 The Dialog Corp. All rts. reserv.
08065830 94131577 PMID: 7507893
Neutralizing antibodies and immunoprotection against pertussis and tetanus obtained by use of a recombinant pertussis toxin- tetanus toxin fusion protein.
Boucher P; Sato H; Sato Y; Locht C
Laboratoire de Microbiologie Genetique et Moleculaire, Institut Pasteur de Lille, France.
Infection and immunity (UNITED STATES) Feb 1994, 62 (2) p449-56, ISSN 0019-9567 Journal Code: 0246127
Document type: Journal Article Languages: ENGLISH Main Citation Owner: NLM Record type: Completed
The currently available diphtheria- tetanus -whole-cell pertussis (DTP) vaccines are associated with a variety of problems, including undesirable side effects and inconsistent efficacy. These problems are probably related to the poor definition of such vaccines, especially with respect to the whole-cell component against pertussis. Ideal vaccines should include only immunoprotective antigens with no toxin activity. As an initial step towards obtaining a well-defined and simplified DTP vaccine, a pertussis toxin- tetanus toxin chimeric protein was constructed. A soluble form of the pertussis toxin S1 subunit was fused to the protective fragment C of tetanus toxin, and the recombinant hybrid protein was produced in Escherichia coli. The 75-kDa fusion protein (p75) was overexpressed as a soluble molecule and purified to near homogeneity by two consecutive chromatographic steps. Purified p75 retained its ability to bind to ganglioside GT1b, the receptor for tetanus toxin, and to be recognized by protective and neutralizing anti-pertussis toxin antibodies specific for conformational epitopes. When administered to mice, the hybrid protein was found to be nontoxic but immunogenic. In addition, it was capable of inducing strong protection against tetanus and some protection against pertussis, as well as eliciting a pertussis toxin-neutralizing antibody response. Although the levels of anti-pertussis toxin antibodies were rather low, neutralizing titers of the immunized mice correlated well with anti-pertussis toxin titers, indicating that protective epitopes are conserved in the recombinant protein. Record Date Created: 19940304 Record Date Completed: 19940304

23/7/1 DIALOG(R)File 155:MEDLINE(R) (c) format only 2004 The Dialog Corp. All rts. reserv.
11119318 97413668 PMID: 9270054
Postischemic infusion of Cu/Zn superoxide dismutase or SOD:Tet451 reduces cerebral infarction following focal ischemia/reperfusion in rats.
Francis J W ; Ren J; Warren L; Brown R H; Finklestein S P
Cecil B. Day Laboratory for Neuromuscular Research, Massachusetts General Hospital, Charlestown 02129, USA.
Experimental neurology (UNITED STATES) Aug 1997, 146 (2) p435-43, ISSN 0014-4886 Journal Code: 0370712
Contract/Grant No.: 1P01AG12992-01; AG; NIA; 1P01NS31248-04; NS; NINDS; P01 NS 10828; NS; NINDS
Document type: Journal Article Languages: ENGLISH Main Citation Owner: NLM Record type: Completed
Oxygen-free radicals play a major role in neuronal cell injury following cerebral ischemia/reperfusion. The free-radical scavenging enzyme, Cu/Zn superoxide dismutase (SOD-1), ameliorates various types of brain injury resulting from temporary CNS ischemia. We have compared the cerebroprotective properties of human SOD-1 (hSOD-1) with a novel recombinant SOD-1 hybrid protein, SOD:Tet451, composed of hSOD-1 linked to the neuronal binding fragment of tetanus toxin (TTxC). Following of temporary middle cerebral artery occlusion, rats infused with equivalent activities of either hSOD-1 or SOD:Tet451 for the initial 3 h of reperfusion showed reductions in cerebral infarct volume of 43 and 57%, respectively, compared to saline-treated controls ($P < 0.01$). Serum hSOD-1 concentrations in rats receiving SOD:Tet451 were seven-fold higher than those in rats receiving the native enzyme. Animals treated with SOD:Tet451 also demonstrated an extended persistence of hSOD-1 in the bloodstream during drug washout as compared to animals given free enzyme. Immunohistochemical examination of brain sections from an SOD:Tet451-treated ischemic rat showed positive immunoreactivity in the ipsilateral cerebral cortex using eit anti-TTxC or anti-human SOD-1 antibodies. Our results document that both hSOD-1 and SOD:Tet451 significantly reduce bra infarct volume in a model of transient focal ischemia/reperfusion in rats. Additionally, our findings suggest that the cerebroprotective effects of SOD-1 may be enhanced by neuronal targeting as seen with the hybrid protein SOD:Tet451. Reco Date Created: 19970919 Record Date Completed: 19970919

23/7/2 DIALOG(R)File 155:MEDLINE(R) (c) format only 2004 The Dialog Corp. All rts. reserv.
11059318 97413668 PMID: 9270054
Postischemic infusion of Cu/Zn superoxide dismutase or SOD:Tet451 reduces cerebral infarction following focal ischemia/reperfusion in rats.
Francis J W ; Ren J; Warren L; Brown R H; Finklestein S P
Cecil B. Day Laboratory for Neuromuscular Research, Massachusetts General Hospital, Charlestown 02129, USA.
Experimental neurology (UNITED STATES) Aug 1997, 146 (2) p435-43, ISSN 0014-4886 Journal Code: 0370712
Contract/Grant No.: 1P01AG12992-01; AG; NIA; 1P01NS31248-04; NS; NINDS; P01 NS 10828; NS; NINDS
Document type: Journal Article Languages: ENGLISH Main Citation Owner: NLM Record type: Completed
Oxygen-free radicals play a major role in neuronal cell injury following cerebral ischemia/reperfusion. The free-radical scavenging enzyme, Cu/Zn superoxide dismutase (SOD-1), ameliorates various types of brain injury resulting from temporary CNS ischemia. We have compared the cerebroprotective properties of human SOD-1 (hSOD-1) with a novel recombinant SOD hybrid protein, SOD:Tet451, composed of hSOD-1 linked to the neuronal binding fragment of tetanus toxin (TTxC). Following of temporary middle cerebral artery occlusion, rats infused with equivalent activities of either hSOD-1 or SOD:Tet451 for the initial 3 h of reperfusion showed reductions in cerebral infarct volume of 43 and 57%, respectively, compared to saline-treated controls ($P < 0.01$). Serum hSOD-1 concentrations in rats receiving SOD:Tet451 were seven-fold higher than those in rats receiving the native enzyme. Animals treated with SOD:Tet451 also demonstrated an extended persistence of hSOD-1 in the bloodstream during drug washout as compared to animals given free enzyme. Immunohistochemical examination of brain sections from an SOD:Tet451-treated ischemic rat showed positive immunoreactivity in the ipsilateral cerebral cortex using eit anti-TTxC or anti-human SOD-1 antibodies. Our results document that both hSOD-1 and SOD:Tet451 significantly reduce bra infarct volume in a model of transient focal ischemia/reperfusion in rats. Additionally, our findings suggest that the cerebroprotective effects of SOD-1 may be enhanced by neuronal targeting as seen with the hybrid protein SOD:Tet451. Reco Date Created: 19970919 Record Date Completed: 19970919

23/7/3 DIALOG(R)File 155:MEDLINE(R) (c) format only 2004 The Dialog Corp. All rts. reserv.
08990056 20281858 PMID: 10820215
Enhancement of diphtheria toxin potency by replacement of the receptor binding domain with tetanus toxin C-fragment: potential vector for delivering heterologous proteins to neurons.
Francis J W ; Brown R H; Figueiredo D; Remington M P; Castillo O; Schwarzschild M A; Fishman P S; Murphy J R; vanderSpek J C
Cecil B. Day Center for Neuromuscular Research, Department of Neurology, Massachusetts General Hospital and Harvard Medical School, Charlestown, MA 02129, USA. francis@helix.mgh.harvard.edu
Journal of neurochemistry (UNITED STATES) Jun 2000, 74 (6) p2528-36, ISSN 0022-3042 Journal Code: 2985190R
Contract/Grant No.: 1P01NS31248-02; NS; NINDS; 5F32HS10064; HS; AHCPR; R01 NS38679-01; NS; NINDS
Document type: Journal Article Languages: ENGLISH Main Citation Owner: NLM Record type: Completed
This study describes the expression, purification, and characterization of a recombinant fusion toxin, DAB(389)TTC, compose of the catalytic and membrane translocation domains of diphtheria toxin (DAB(389)) linked to the receptor binding fragment of tetanus toxin (C-fragment). As determined by its ability to inhibit cellular protein synthesis in primary neuron cultures, DAB(389)TTC was approximately 1,000-fold more cytotoxic than native diphtheria toxin or the previously described fusion toxi DAB(389)MSH. The cytotoxic effect of DAB(389)TTC on cultured cells was specific toward neuronal-type cells and was blocke by coincubation of the chimeric toxin with tetanus antitoxin. The toxicity of DAB(389)TTC, like that of diphtheria toxin, was dependent on passage through an acidic compartment and ADP-ribosyltransferase activity of the DAB(389) catalytic fragment These results suggest that a catalytically inactive form of DAB(389)TTC may be useful as a nonviral vehicle to deliver exogeno proteins to the cytosolic compartment of neurons. Record Date Created: 20000602 Record Date Completed: 20000602
Tags: Animal; Human; Support, Non-U.S. Gov't; Support, U.S. Gov't, Non-P.H.S.; Support, U.S. Gov't, P.H.S. Descriptors: Hippocampus--metabolism--ME; *Immunotoxins--metabolism--ME; *Neurons--metabolism--ME; *Peptide Fragments--metabolism--ME; *Superoxide Dismutase metabolism--ME; * Tetanus Toxin--metabolism--ME; Base Sequence; Biological Transport; Blotting, Western; Cell Line; Cells, Cultured; Cloning Molecular; DNA Primers; Electrophoresis, Polyacrylamide Gel; Immunohistochemistry; Immunotoxins--administration and dosage--AD; Kinetics Molecular Sequence Data; Peptide Fragments--administration and dosage--AD ; Peptide Fragments--biosynthesis--BI; Polymerase Chain Reaction; Protein Hybridization; Rats; Restriction Mapping; Superoxide Dismutase --administration and dosage--AD; Superoxide Dismutase--

biosynthesis--BI; Tetanus Toxin--administration and dosage--AD; Tetanus Toxin --biosynthesis--BI CAS Registry No.: 0 (DNA Primers); 0 (Immunotoxins); 0 (Peptide Fragments); 0 (Tetanus Toxin); 0 (tetanus toxin fragment C) Enzyme No.: EC 1.15.1.1 (Superoxide Dismutase)

23/6/4 08629590 95318117 PMID: 7797532
CuZn superoxide dismutase (SOD-1): tetanus toxin fragment C hybrid protein for targeted delivery of SOD-1 to neuronal cells. Jun 23 1995

09jan04 12:55:17 User208600 Session D1604.3
File 34:SciSearch(R) Cited Ref Sci 1990-2004/Jan W1 (c) 2004 Inst for Sci Info
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E2 1 CR=FRANCIS J, 1994, V99, P395, J GEOPHYS RES
E3 0 *CR=FRANCIS J, 1995
E4 1 CR=FRANCIS J, 1995, BERICHT KARTZFEHN
E5 1 CR=FRANCIS J, 1995, BLOOD CONSERVATION A
E6 1 CR=FRANCIS J, 1995, P26, WORLD INGRED MAR
E7 1 CR=FRANCIS J, 1995, P34, WORLD INGREDIENT SEP
E8 2 CR=FRANCIS J, 1995, P7, TRANSFORMATION TROPI
E9 1 CR=FRANCIS J, 1995, V19, P383, J ACCOUNT ECON
E10 1 CR=FRANCIS J, 1995, V329, P208, NEW ENGL J MED
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E15 1 CR=FRANCIS J, 1996, P326, NATURAL FOOD COLORAN
E16 1 CR=FRANCIS J, 1996, P67, IMPROVING RUMINANT P
E17 3 CR=FRANCIS J, 1996, P917, GERIATRIC MED
E18 1 CR=FRANCIS J, 1996, V125, P421, ANN INTERN MED
E19 6 CR=FRANCIS J, 1996, V5, P103, CNS DRUGS
E20 1 CR=FRANCIS J, 1996, V77, PS290, OXYGEN ISOTOPIC Z
E21 1 CR=FRANCIS J, 1996, V9, P881, COLLOID SURF A
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E23 1 CR=FRANCIS J, 1997, J PROCESSES MECH ENG
E24 1 CR=FRANCIS J, 1997, JOURNEY ARUSHA SEYCH

Ref Items Index-term
E1 3 CR=FRANCIS JW, 1996, V112, P317, J MOL CATAL A-CH
E2 1 CR=FRANCIS JW, 1996, V26, P192, J COLL SCI TEACH
E3 0 *CR=FRANCIS JW, 1997
E4 12 CR=FRANCIS JW, 1997, V146, P435, EXP NEUROL
E5 1 CR=FRANCIS JW, 1997, V23, SOC NEUR ABSTR
E6 29 CR=FRANCIS JW, 1998, V95, P6492, P NATL ACAD SCI
E7 2 CR=FRANCIS JW, 2000, V62, P90, AM BIOL TEACH
E8 7 CR=FRANCIS JW, 2000, V74, P2528, J NEUROCHEM
E9 1 CR=FRANCIS K, UNPUB
E10 1 CR=FRANCIS K, V92, P3616, BLOOD
E11 1 CR=FRANCIS K, 1955, V45, AM J PUBLIC HLTH 2 S
E12 1 CR=FRANCIS K, 1971, NZ KIWI

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E1 1 CR=FRANCIS JW, 1994, V17, P7, NEUROTOXICOL TERATO
E2 1 CR=FRANCIS JW, 1994, V56, P484, AM BIOL TEACH
E3 0 *CR=FRANCIS JW, 1995
E4 25 CR=FRANCIS JW, 1995, V17, P7, NEUROTOXICOL TERATO
E5 2 CR=FRANCIS JW, 1995, V270, P15432, J BIOL CHEM
E6 22 CR=FRANCIS JW, 1995, V270, P15434, J BIOL CHEM
E7 1 CR=FRANCIS JW, 1995, V270, P5434, J BIOL CHEM
E8 1 CR=FRANCIS JW, 1995, V99, P77, J MOL CATAL
E9 13 CR=FRANCIS JW, 1995, V99, P77, J MOL CATAL A-CHEM
E10 1 CR=FRANCIS JW, 1996, V101, P317, J MOL CATAL A-CH
E11 3 CR=FRANCIS JW, 1996, V112, P317, J MOL CATAL A-CH
E12 1 CR=FRANCIS JW, 1996, V26, P192, J COLL SCI TEACH
E13 12 CR=FRANCIS JW, 1997, V146, P435, EXP NEUROL
E14 1 CR=FRANCIS JW, 1997, V23, SOC NEUR ABSTR
E15 29 CR=FRANCIS JW, 1998, V95, P6492, P NATL ACAD SCI
E16 2 CR=FRANCIS JW, 2000, V62, P90, AM BIOL TEACH
E17 7 CR=FRANCIS JW, 2000, V74, P2528, J NEUROCHEM
E18 1 CR=FRANCIS K, UNPUB
E19 1 CR=FRANCIS K, V92, P3616, BLOOD
E20 1 CR=FRANCIS K, 1955, V45, AM J PUBLIC HLTH 2 S
E21 1 CR=FRANCIS K, 1971, NZ KIWI
E22 1 CR=FRANCIS K, 1979, V35, P23, EXPERIENTIA
E23 1 CR=FRANCIS K, 1982, V52, P11, P NAT ACAD SCI IND
E24 6 CR=FRANCIS K, 1985, V26, P1195, PLANT CELL PHYSIO

S1 50 E4-E7
S2 159230 FUS?
S3 11 S1 AND S2
S4 254001 CHIMER? OR HYBRID?
S5 4 S1 AND S4 NOT S3

3/6/1 11080385 Genuine Article#: 602XU Number of References: 129
Title: Clostridial neurotoxins (ABSTRACT AVAILABLE) Publication date: 20020000

3/6/2 09710099 Genuine Article#: 437QE Number of References: 58
Title: Neuronal targeting of cardiotrophin-1 by coupling with tetanus toxin C fragment (ABSTRACT AVAILABLE) Publication date: 20010500

3/6/3 08930221 Genuine Article#: 345QX Number of References: 46
Title: Protective effect of supplemental superoxide dismutase on survival of neuronal cells during starvation - Requirement for cytosolic distribution (ABSTRACT AVAILABLE) Publication date: 20000600

3/6/4 08657931 Genuine Article#: 312XG Number of References: 52
Title: Enhancement of diphtheria toxin potency by replacement of the receptor binding domain with tetanus toxin C-fragment: A potential vector for delivering heterologous proteins to neurons (ABSTRACT AVAILABLE) Publication date: 20000600

3/6/5 08604608 Genuine Article#: 306PP Number of References: 26
Title: High-level expression of tetanus toxin fragment C-thioredoxin fusion protein in Escherichia coli (ABSTRACT AVAILABLE) Publication date: 20000400

3/6/6 08346824 Genuine Article#: 274MM Number of References: 41
Title: A somatic gene transfer approach using recombinant fusion proteins to map muscle-motoneuron projections in Xenopus spinal cord (ABSTRACT AVAILABLE) Publication date: 19991100

3/6/7 07482407 Genuine Article#: 171LB Number of References: 149
Title: Tetanus and botulinum neurotoxins: mechanism of action and therapeutic uses (ABSTRACT AVAILABLE) Publication date: 19990228

3/6/8 07199828 Genuine Article#: 135NQ Number of References: 42
Title: Tracing axons (ABSTRACT AVAILABLE) Publication date: 19981000

3/6/9 06177475 Genuine Article#: YA203 Number of References: 30
Title: Structure of the receptor binding fragment H-C of tetanus neurotoxin (ABSTRACT AVAILABLE) Publication date: 19971000

3/6/10 06055012 Genuine Article#: XR765 Number of References: 41
Title: Construction of hybrid proteins that migrate retrogradely and transsynaptically into the central nervous system (ABSTRACT AVAILABLE) Publication date: 19970819

3/6/11 05946700 Genuine Article#: XJ537 Number of References: 50
Title: Delivery of recombinant tetanus-superoxide dismutase proteins to central nervous system neurons by retrograde axonal transport (ABSTRACT AVAILABLE) Publication date: 19970600

3/7/7 DIALOG(R)File 34:SciSearch(R) Cited Ref Sci (c) 2004 Inst for Sci Info. All rts. reserv.
07482407 Genuine Article#: 171LB Number of References: 149
Title: Tetanus and botulinum neurotoxins: mechanism of action and therapeutic uses
Author(s): Pellizzari R; Rossetto O; Schiavo G; Montecucco C (REPRINT)
Corporate Source: UNIV PADUA,CTR BIOMEMBRANE, CNR, VIA G COLOMBO 3/I-35100 PADUA//ITALY/ (REPRINT); UN PADUA,CTR BIOMEMBRANE, CNR/I-35100 PADUA//ITALY/; UNIV PADUA,DIPARTIMENTO SCI BIOMED/I-35100 PADUA//ITALY/ ; IMPERIAL CANC RES FUND,LAB NEUROBIOPATHOL/LONDON WC2A 3PX//ENGLAND/
Journal: PHILOSOPHICAL TRANSACTIONS OF THE ROYAL SOCIETY OF LONDON SERIES B-BIOLOGICAL SCIENCES 1999, V354, N1381 (FEB 28), P259-268 ISSN: 0962-8436 Publication date: 19990228
Publisher: ROYAL SOC LONDON, 6 CARLTON HOUSE TERRACE, LONDON SW1Y 5AG, ENGLAND
Language: English Document Type: ARTICLE
Abstract: The clostridial neurotoxins responsible for tetanus and botulism are proteins consisting of three domains endowed w different functions: neurospecific binding, membrane translocation and proteolysis for specific components of the neuroexocytosis apparatus. Tetanus neurotoxin (TeNT) binds to the presynaptic membrane of the neuromuscular junction, is internalized and transported retroaxonally to the spinal cord. The spastic paralysis induced by the toxin is due to the blockade neurotransmitter release from spinal inhibitory interneurons. In contrast, the seven serotypes of botulinum neurotoxins (BoNT act at the periphery by inducing a flaccid paralysis due to the inhibition of acetylcholine release at the neuromuscular junction TeNT and BoNT serotypes B, D, F and G cleave specifically at single but different peptide bonds, of the vesicle associated membrane protein (VAMP) synaptobrevin, a membrane protein of small synaptic vesicles (SSVs). BoNT types A, C and E cleave SNAP-25 at different sites located within the carboxyl-terminus, while BoNT type C: additionally cleaves syntaxin. The remarkable specificity of BoNTs is exploited in the treatment of human diseases characterized by a hyperfunction of choliner terminals.

3/7/11 DIALOG(R)File 34:SciSearch(R) Cited Ref Sci (c) 2004 Inst for Sci Info. All rts. reserv.
05946700 Genuine Article#: XJ537 Number of References: 50
Title: Delivery of recombinant tetanus-superoxide dismutase proteins to central nervous system neurons by retrograde axona transport

Author(s): Figueiredo DM; Hallewell RA (REPRINT) ; Chen LL; Fairweather NF; Dougan G; Savitt JM; Parks DA; Fishman PS
Corporate Source: UNIV LONDON IMPERIAL COLL SCI TECHNOL & MED,DEPT BIOCHEM/LONDON SW7 2AZ//ENGLAND/ (REPRINT); UNIV LONDON IMPERIAL COLL SCI TECHNOL & MED,DEPT BIOCHEM/LONDON SW7 2AZ//ENGLAND/; UNIV MARYLAND,SCH MED, VAMC, NEUROL SERV/BALTIMORE//MD/21201; UNIV MARYLAND,SCH MED, VAMC, DEPT NEUROL/BALTIMORE//MD/21201
Journal: EXPERIMENTAL NEUROLOGY, 1997, V145, N2 (JUN), P546-554 ISSN: 0014-4886 Publication date: 19970600
Publisher: ACADEMIC PRESS INC JNL-COMP SUBSCRIPTIONS, 525 B ST, STE 1900, SAN DIEGO, CA 92101-4495
Language: English Document Type: ARTICLE
Abstract: The nontoxic C fragment of tetanus toxin (TC) can transport other proteins from the circulation to central nervous system (CNS) motor neurons. Increased levels of CuZn superoxide dismutase (SOD) are protective in experimental models of stroke and Parkinson's disease, whereas mutations in SOD can cause motor neuron disease. We have linked TC to SOD and purified the active recombinant proteins in both the TC-SOD and SOD-TC orientations. Light microscopic immunohistochemistry and quantitative enzyme-linked immunosorbant assays (ELISA) of mouse brainstem, after intramuscular injection, demonstrate that the fusion proteins undergo retrograde axonal transport and transsynaptic transfer as efficiently as TC alone. (C) 1997 Academic Press.

5/6/1 09361245 Genuine Article#: 396BM Number of References: 39
Title: I nteraction of tetanus toxin derived hybrid proteins with neuronal cells (ABSTRACT AVAILABLE) Publication date: 20001100

5/6/2 07912310 Genuine Article#: 223EZ Number of References: 43
Title: Hybrid enzymes (ABSTRACT AVAILABLE) Publication date: 19990800

5/6/3 07467070 Genuine Article#: 169FN Number of References: 35
Title: Non-viral neuronal gene delivery mediated by the H-C fragment of tetanus toxin (ABSTRACT AVAILABLE) Publication date: 19990200

5/6/4 06042440 Genuine Article#: XR256 Number of References: 47
Title: Postischemic infusion of Cu/Zn superoxide dismutase or SOD:Tet451 reduces cerebral infarction following focal ischemia/reperfusion in rats (ABSTRACT AVAILABLE) Publication date: 19970800

5/7/2 DIALOG(R)File 34:SciSearch(R) Cited Ref Sci (c) 2004 Inst for Sci Info. All rts. reserv.
07912310 Genuine Article#: 223EZ Number of References: 43
Title: Hybrid enzymes
Author(s): Beguin P (REPRINT)
Corporate Source: INST PASTEUR,DEPT BIOTECHNOL, UNITE PHYSIOL CELLULAIRE, 28 RUE DR ROUX/F-75724 PAR 15//FRANCE/ (REPRINT)
Journal: CURRENT OPINION IN BIOTECHNOLOGY, 1999, V10, N4 (AUG), P336-340 ISSN: 0958-1669 Publication date: 19990800 Publisher: CURRENT BIOLOGY LTD, 34-42 CLEVELAND STREET, LONDON W1P 6LE, ENGLAND
Language: English Document Type: REVIEW
Abstract: Combining structural elements belonging to different proteins is a powerful method for generating proteins with new properties. Progress based on detailed structural and functional analysis enables a better integration of the elements to be fit together while preserving or creating functional interactions between them.

5/7/3 DIALOG(R)File 34:SciSearch(R) Cited Ref Sci (c) 2004 Inst for Sci Info. All rts. reserv.
07467070 Genuine Article#: 169FN Number of References: 35
Title: Non-viral neuronal gene delivery mediated by the H-C fragment of tetanus toxin
Author(s): Knight A (REPRINT) ; Carvajal J; Schneider H; Coutelle C; Chamberlain S; Fairweather N
Corporate Source: UNIV LONDON IMPERIAL COLL SCI TECHNOL & MED,SCH MED, CYST FIBROSIS GENE THERAPY RES GRP/LONDON SW7 2AZ//ENGLAND/ (REPRINT); UNIV LONDON IMPERIAL COLL SCI TECHNOL & MED,SCH MED GENE THERAPY RES GRP, SECT MOL GENET/LONDON//ENGLAND/; UNIV LONDON IMPERIAL COLL SCI TECHNOL & MED,SCH MED, ATAXIA GRP, SECT MOL GENET, DIV BIOMED SCI/LONDON//ENGLAND/; UNIV LONDON IMPERIAL COLL SCI TECHNOL & MED,DEPT BIOCHEM/LONDON//ENGLAND/
Journal: EUROPEAN JOURNAL OF BIOCHEMISTRY, 1999, V259, N3 (FEB), P762-769 ISSN: 0014-2956 Publication date: 19990200 Publisher: SPRINGER VERLAG, 175 FIFTH AVE, NEW YORK, NY 10010 Language: English Document Type: ARTICLE
Abstract: Many inherited neurological diseases and cancers could potentially benefit from efficient targeted gene delivery to neurons of the central nervous system. The nontoxic fragment C (H-C) of tetanus toxin retains the specific nerve cell binding and transport properties of tetanus holotoxin. The H-C fragment has previously been used to promote the uptake of attached proteins such as horseradish peroxidase, beta-galactosidase and superoxide dismutase into neuronal cells in vitro and in viv We report the use of purified recombinant H-C fragment produced in yeast and covalently bound to polylysine [poly(K)] to enable binding of DNA. We demonstrate that when used to transfect cells, this construct results in nonviral gene delivery and marker gene expression in vitro in N18 RE 105 cells (a neuroblastoma x glioma mouse/rat hybrid cell line) and F98 (a gliom cell line). Transfection was dependent on H-C and was neuronal cell type specific. H-C may prove a useful targeting ligand fo future neuronal gene therapy

Mark a special word or phrase in this record: Mark!

Select one or more organism in this record: All organism
Clostridium tetani
Submit

EC NUMBER COMMENTARY
3.4.24.68 -

RECOMMENDED NAME GeneOntology No.
Tentoxilysin GO:0000000

SYSTEMATIC NAME
No entries in this field

SYNONYMS	ORGANISM	COMMENTARY	LITERATURE
More	-	cf. EC 3.4.24.69	-
Tentoxylysin	-	SwissProt	-
Tetanus neurotoxin	-	-	-

CAS REGISTRY NUMBER COMMENTARY
107231-12-9 -

REACTION	COMMENTARY
Synaptobrevin + H2O = hydrolyzed synaptobrevin	Clostridium tetani: structure and mechanism <2, 5, 6>

REACTION TYPE	ORGANISM	COMMENTARY	LITERATURE
hydrolysis of peptide bond	-	-	-

ORGANISM	COMMENTARY	LITERATURE
Clostridium tetani	toxigenic strains N3911 <1>; E 88 (non-sporulating) <3>; Harvard <6>; all toxigenic strains synthesize only one type of neurotoxin <5, 6>	1-6

SUBSTRATE	PRODUCT	REACTION DIAGRAM	ORGANISM	COMMENTARY/ Substrate r:=reversible ir:=irreversible	LITERATURE/ Substrate	COMMENTARY/ Product	LITERATURE/ Product
More	**?**		Clostridium tetani	no substrates are rat <4,5>; or chicken <5>; synaptobrevin-1 (with Val76 instead of Gln76) or short peptides containing the cleavage site of the target protein <5,6>; catalytic activity requires reduction of the single interchain disulfide bond of the neurotoxin <4> i.e. VAMP <5,6>; neuronal vesicle-associated	4, 5, 6	-	-

Synaptobrevin + H2O	**Hydrolyzed synaptobrevin**		Clostridium tetani	membrane protein, MW 19000 <4>; with 2 isoforms in human <4>; chicken <5>; or rat brain <4,5>; : synaptobrevin/VAMP-1 and synaptobrevin/VAMP-2, cleaves at Gln76-Phe77, the same site as botulin neurotoxin B <5,6>	1 , 2 , 3 , 4 , 5 , 6	2 peptide fragments, MW 12000 and MW 7000	4	

NATURAL SUBSTRATE	NATURAL PRODUCT	REACTION DIAGRAM	ORGANISM	COMMENTARY SUBSTRATE	LITERATURE (Substrate)	COMMENTARY PRODUCT	LITERATURE (Product)	ORGANISM (Product)
Synaptobrevin + H2O	-		Clostridium tetani	i.e. VAMP, neuronal vesicle-associated membrane protein, predominantly exposed to cytosol <5>; neurotoxin blocks neurotransmitter release in Aplysia neurons <4>; tetanus neurotoxin receptors are located on the motor neuron plasmalemma at neuromuscular junction, after binding the toxin is internalized inside vesicles of unknown nature and then translocated across the vesicle membrane <5>; enzyme disables neuroexocytosis apparatus, acts at spinal inhibitory interneurons, blocking release of various neurotransmitters to produce spastic paralysis, clostridial neurotoxins are described as the most toxic substances known	4 , 5 , 6	-	-	-

COFACTOR	ORGANISM	COMMENTARY	LITERATURE	IMAGE
No entries in this field				

METAL IONS	ORGANISM	COMMENTARY	LITERATURE
Cobalt	Clostridium tetani	zinc-dependent endoproteinase, can replace zinc	5
Nickel	Clostridium tetani	zinc-dependent endoproteinase, can replace zinc	5
Zinc	Clostridium tetani	zinc-dependent endoproteinase <2,4,5,6>; L-chain: form of zinc-endopeptidase, 0.8-1 gatom zinc/mol toxin, bound to light or L-chain <6>; 1 atom zinc per molecule toxin, zinc-binding motif: His-Glu-X-X-His, nickel or cobalt can replace zinc <5>; toxin surface topography of His-residues <2>	2 , 4 , 5 , 6

INHIBITORS	ORGANISM	COMMENTARY	LITERATURE	IMAGE
Ala-Ser-Gln-Phe-Glu-Thr-Ser	Clostridium tetani	synthetic peptide containing cleavage site of synaptobrevin, inhibits toxin action on buccal ganglion of Aplysia californica	4	● 2D-image
	Clostridium			● 2D-

Captopril	tetani	-	4 , 5	image
EDTA	Clostridium tetani	-	4 .	2D-image
Gln-Phe-Glu-Thr	Clostridium tetani	synthetic peptide containing cleavage site of synaptobrevin, inhibits toxin action on buccal ganglion of Aplysia californica	4	2D-image
NaOCl	Clostridium tetani	inactivation	6	2D-image

ACTIVATING COMPOUND	ORGANISM	COMMENTARY	LITERATURE	IMAGE
Proteases	Clostridium tetani	activation by rapid cleavage within an exposed loop of the single inactive MW 150000 polypeptide chain and generation of active di-chain neurotoxin <5,6>; bacterial <5,6>; or tissue proteases <5>	5,6	-

KM VALUE [mM] KM VALUE [mM] Maximum SUBSTRATE ORGANISM COMMENTARY LITERATURE IMAGE

No entries in this field

Ki VALUE [mM] Ki VALUE [mM] Maximum INHIBITOR ORGANISM COMMENTARY LITERATURE IMAGE

No entries in this field

TURNOVER NUMBER TURNOVER NUMBER MAXIMUM SUBSTRATE ORGANISM COMMENTARY LITERATURE IMAGE

No entries in this field

SPECIFIC ACTIVITY [µM/min/mg]	SPECIFIC ACTIVITY MAXIMUM	ORGANISM	COMMENTARY	LITERATURE
additional information	-	Clostridium tetani	in neurotoxin-injected Aplysia neurons 4-10 molecules of L-chains are sufficient to cause blockade of neurotransmitter release with a t1/2 of 20-40 min at 20°C	5

pH OPTIMUM pH MAXIMUM ORGANISM COMMENTARY LITERATURE

No entries in this field

pH RANGE pH RANGE MAXIMUM ORGANISM COMMENTARY LITERATURE

No entries in this field

TEMPERATURE OPTIMUM	TEMPERATURE OPTIMUM MAXIMUM	ORGANISM	COMMENTARY	LITERATURE
37	-	Clostridium tetani	assay at	4 , 6

TEMPERATURE RANGE TEMPERATURE MAXIMUM ORGANISM COMMENTARY LITERATURE

No entries in this field

SOURCE TISSUE	ORGANISM	COMMENTARY	LITERATURE
culture supernatant	Clostridium tetani	-	6

LOCALIZATION	ORGANISM	COMMENTARY	GeneOntology No.	LITERATURE
cytosol	Clostridium tetani	accumulates until bacterial lysis	GO:0005829	5 , 6

ACCESSION CODE ENTRY NAME ORGANISM NO. OF AA MOLECULAR WEIGHT[Da] SOURCE Sequence

No entries in this field

PDB	ORGANISM
1A8D, download	Clostridium tetani

1AF9, download Clostridium tetani

1DFQ, download Clostridium tetani

1DIW, download Clostridium tetani

1DLL, download Clostridium tetani

1FV2, download Clostridium tetani

MOLECULAR WEIGHT	MOLECULR WEIGHT MAXIMUM	ORGANISM	COMMENTARY	LITERATURE
150700	-	Clostridium tetani	Clostridium tetani, calculated from amino acid sequence	6
additional information	- -	Clostridium tetani	amino acid sequence homologies between tetanus toxin TeNT and botulinum toxins BoNT/A, B and E	3

SUBUNITS	ORGANISM	COMMENTARY	LITERATURE
More	Clostridium tetani	the enzyme consists of a heavy (H) chain and a light (L) chain <2,3>; held together by a single disulfide bond and non-covalent forces <2>; MW 52288 (L-chain) and MW 98300 (H-chain), calculated from amino acid sequence <3>	2 , 3

POSTTRANSLATIONAL MODIFICATION ORGANISM COMMENTARY LITERATURE

No entries in this field

Crystallization/COMMENTARY ORGANISM LITERATURE

No entries in this field

pH STABILITY pH STABILITY MAXIMUM ORGANISM COMMENTARY LITERATURE

No entries in this field

TEMPERATURE STABILITY TEMPERATURE STABILITY MAXIMUM ORGANISM COMMENTARY LITERATURE

No entries in this field

GENERAL STABILITY ORGANISM LITERATURE

No entries in this field

ORGANIC SOLVENT ORGANISM COMMENTARY LITERATURE

No entries in this field

OXIDATION STABILITY	ORGANISM	LITERATURE
-	Clostridium tetani	6

STORAGE STABILITY	ORGANISM	COMMENTARY	LITERATURE
-80°C, in 10 mM HEPES buffer, pH 7.2, 50 mM NaCl, after freezing in liquid N2, stable	Clostridium tetani	-	6

Purification/COMMENTARY	ORGANISM	LITERATURE
single-chain, two-chain and L-chain form <6>; very toxic! Booster injection of tetanus toxoid before starting research with tetanus toxin advisable, human anti-tetanus neurotoxin antibodies available <6>	Clostridium tetani	2 , 6

Cloned/COMMENTARY	ORGANISM	LITERATURE
Clostridium tetani <1,3>; expressed in Escherichia coli JM101 using three different plasmid vectors <3>	Clostridium tetani	1 , 3

ENGINEERING ORGANISM COMMENTARY LITERATURE

No entries in this field

Renatured/COMMENTARY ORGANISM LITERATURE

No entries in this field

APPLICATION ORGANISM COMMENTARY LITERATURE

No entries in this field

DISEASE TITLE OF PUBLICATION LINK TO PUBMED

No entries in this field

REF.	AUTHORS	TITLE	JOURNAL	VOL.	PAGES	YEAR	ORGANISM	COMMENTARY	LINK TO PUBMED
1	Fairweather, N.F.; Lyness, V.A.	**The complete nucleotide sequence of tetanus toxin**	Nucleic Acids Res.	14	7809-7813	1986	Clostridium tetani	-	PubMed
2	Rossetto, O.; Schiavo, G.; Polverino de Laureto, P.; Fabbiani, S.; Montecucco, C.	**Surface topography of histidine residues of tetanus toxin probed by immobilized-metal-ion affinity chromatography**	Biochem. J.	285	9-12	1992	Clostridium tetani	-	PubMed
3	Eisel, U.; Jarusch, W.; Goretzki, K.; Henschen, A.; Engels, J.; Weller, U.; Hudel, M.; Habermann, E.; Niemann, H.	**Tetanus toxin: primary structure, expression in E. coli, and homology with botulinum toxins**	EMBO J.	5	2495-2502	1986	Clostridium tetani	-	PubMed
4	Schiavo, G.; Benfenati, F.; Poulain, B.; Rossetto, O.; Polverino de Laureto, P.; DasGupta, B.R.; Montecucco, C.	**Tetanus and botulinum-B neurotoxins block neurotransmitter release by proteolytic cleavage of synaptobrevin [see comments]**	Nature	359	832-835	1992	Clostridium tetani	-	PubMed
5	Montecucco, C.; Schiavo, G.	**Mechanism of action of tetanus and botulinum neurotoxins**	Mol. Microbiol.	13	1-8	1994	Clostridium tetani	review	PubMed
6	Schiavo, G.; Montecucco, C.	**Tetanus and botulism neurotoxins: isolation and assay**	Methods Enzymol.	248	643-652	1995	Clostridium tetani	review	PubMed

LINKS TO OTHER DATABASES (specific for EC-Number 3.4.24.68)

ExPASy

Online Mendelian Inheritance in Man

KEGG

NCBI: PubMed, Protein, Nucleotide, Structure, Genome, OMIM, Domains

IUBMB Enzyme Nomenclature

WIT database

EMP Project

PDB database(3D structure)

PROSITE Database of protein families and domains

SYSTERS

Protein Mutant Database

Mark a special word or phrase in this record: Mark!

Select one or more organism in this record:
All organism
Clostridium barati
Clostridium botulinum
Clostridium butyricum
Clostridium sp.
Submit

EC NUMBER	COMMENTARY
3.4.24.69	-

RECOMMENDED NAME	GeneOntology No.
Bontoxilysin	GO:0000000

SYSTEMATIC NAME

No entries in this field

SYNONYMS	ORGANISM	COMMENTARY	LITERATURE
BoNT	-	-	-
BoNT/B	-	SwissProt	-
BoNT/C1	-	SwissProt	-
BoNT/D	-	SwissProt	-
BoNT/E	-	SwissProt	-
BoNT/F	-	SwissProt	-
BoNT/G	-	SwissProt	-
Bontoxilysin C1	-	SwissProt	-
Botulinum neurotoxin	-	-	-
More	-	cf. EC 3.4.24.68	-

CAS REGISTRY NUMBER	COMMENTARY
107231-12-9	-

REACTION	COMMENTARY
Protein + H2O = hydrolyzed protein	Clostridium botulinum: mechanism <4>; Clostridium botulinum, Clostridium barati, Clostridium butyricum: structure/function relationship <5>

REACTION TYPE	ORGANISM	COMMENTARY	LITERATURE
hydrolysis of peptide bond	-	-	-

ORGANISM	COMMENTARY	LITERATURE
Clostridium barati	-	5
Clostridium botulinum	strains 62A (serotype A) or Beluga (serotype E) <10>; type G strain <15>; 7 serologically different neurotoxin types: BoNT/A-G <2, 3, 5, 6>; serotypes BoNT/A, BoNT/B <1, 4, 8, 15>; BoNT/C, BoNT/D <15>; BoNT/E <1, 4, 8>	1-10 , 12 , 15
Clostridium butyricum	-	5
Clostridium sp.	serotypes BoNT/A, B, D, E <13>; F <13, 14>	6 , 11 , 13 , 14

COMMENTARY/

SUBSTRATE	PRODUCT	REACTION DIAGRAM	ORGANISM	Substrate r:=reversible ir:=irreversible	LITERATURE/ Substrate	COMMENTARY/ Product	LITERATU Product
More	?		Clostridium botulinum	catalytic activity requires reduction of the single interchain disulfide bond of the neurotoxin <4,15>; activating protease activity is localized on light or L-chain of neurotoxin <4>; the clostridial neurotoxins differ from other proteases in the recognition of the tertiary structure of the target rather than the sequence of the peptide bond to be cleaved <15>; neuroparalytic activity tested by intravenous injection into Balb/c mice <1>; no hydrolysis of short peptides spanning the respective cleavage sites of the target proteins <5,6>; synaptotagmin, synaptophysin <15>	1 , 4 , 5 , 6 , 15	-	-
More	?		Clostridium barati	no hydrolysis of short peptides spanning the respective cleavage sites of the target proteins <5>	5	-	-
More	?		Clostridium butyricum	no hydrolysis of short peptides spanning the respective cleavage sites of the target proteins <5>	5	-	-
More	?		Clostridium sp.	the botulinum neurotoxins are divided into two groups: the A-E type and the B-D-F-tetanus toxin type <13>; no hydrolysis of short peptides spanning the respective cleavage sites of the target proteins <6>; N-ethylmaleimide sensitive factor (i.e. NSF), alpha/beta-SNAP or gamma-SNAP <13>	6 , 13	-	-
Proteins of neuroexocytosis apparatus + H2O	?		Clostridium botulinum	-	2 , 3 , 5 , 6	-	-
Proteins of neuroexocytosis apparatus + H2O	?		Clostridium barati	-	5	-	-
Proteins of neuroexocytosis apparatus + H2O	?		Clostridium butyricum	-	5	-	-
Proteins of neuroexocytosis apparatus + H2O	?		Clostridium sp.	-	6	-	-
Recombinant glutathione S-methyltransferase	Hydrolyzed recombinant glutathione S-		Clostridium	-	15	2 proteolytic fragments. MW	15

VAMP-2 fusion protein + H2O	**methyltransferase VAMP-2 fusion protein**		botulinum			36000 and MW 6000	
Synaptobrevin + H2O	**Hydrolyzed synaptobrevin**		Clostridium botulinum	i.e. VAMP <5,6,12,15>; synaptic vesicle-associated membrane protein <4,6,15>; MW 19000 <4>; two isoforms in human <4>; chicken <5>; or rat brain <4,5>; : synaptobrevin/VAMP-1 (VAMP-1 from chicken, #Clostridium botulinum,5#Clostridium barati,o#Clostridium butyricum# <5> or rat brain, #Clostridium botulinum,n#Clostridium barati,l#Clostridium butyricum# <4, 5> carrying Val76 instead of Gln76 is not hydrolyzed by serotype BoNT/B, #Clostridium botulinum,o#Clostridium barati,i#Clostridium butyricum# <4, 5>) <4,5,15>; and synaptobrevin/VAMP-2 <4,5,6,15>; both isoforms are cleaved at the same rate <15>; highly specific neurotoxins <4,5,6,15>; serotype BoNT/B: cleavage at Ser-Gln-+-Phe-Glu (at the same site as the tetanus neurotoxin) <5>; or Gln76-Phe77 <4>; or Gln-Lys-+-Leu-Ser <5>; or-Asp-Gln-+-Lys-Leu-, serotype BoNT/G: cleavage at Ala83-Ala84 (VAMP-1), Ala81-Ala82 (VAMP-2) <15>; or Ser-Ala-+-Ala-Lys <5>; hydrolyzed by serotypes BoNT/B <4,5,6>; D, F or G <5,6>; in vitro, in synaptosomes and in injected Aplysia neurons <5>; no substrate of serotype BoNT/A or E <4,12>; the term -+- depicts the points of cleavage i.e. VAMP <6,13,14>; synaptic vesicle-associated membrane protein <6,13,14>; : synaptobrevin/VAMP-1 (VAMP-1 from chicken, #Clostridium botulinum,t#Clostridium barati,r#Clostridium butyricum# <5> or rat brain, #Clostridium botulinum,y#Clostridium barati,n#Clostridium butyricum# <4, 5> carrying Val76 instead	**4** , **5** , **6** , **15**	2 proteolytic fragments, MW 12000 and MW 7000 <4>; MW 13000 and MW 6000 <15>	**4** , **15**

				of Gln76 is not hydrolyzed by serotype BoNT/B, #Clostridium botulinum,r#Clostridium barati,n#Clostridium butyricum# <4, 5>) <13>; and synaptobrevin/VAMP-2 <6,13>; both isoforms are cleaved at the same rate <13,14>; highly specific neurotoxins <6,13,14>; serotype BoNT/D: cleavage at Lys61-Leu62 <13>; serotype BoNT/F: cleavage at Gln-Lys <14>; hydrolyzed by serotypes BoNT/B <6>; D, F or G <6>; the term -+- depicts the points of cleavage			
Synaptobrevin + H2O	**Hydrolyzed synaptobrevin**		Clostridium sp.	i.e. VAMP <5>; chicken <5>; or rat brain <5>; : synaptobrevin/VAMP-1 (VAMP-1 from chicken, #Clostridium botulinum,k#Clostridium barati, #Clostridium butyricum# <5> or rat brain, #Clostridium botulinum,o#Clostridium barati,m#Clostridium butyricum# <4, 5> carrying Val76 instead of Gln76 is not hydrolyzed by serotype BoNT/B, #Clostridium botulinum,>#Clostridium barati,e#Clostridium butyricum# <4, 5>) <5>; and synaptobrevin/VAMP-2 <5>; highly specific neurotoxins <5>; serotype BoNT/B: cleavage at Ser-Gln-+-Phe-Glu (at the same site as the tetanus neurotoxin) <5>; or Gln-Lys-+-Leu-Ser <5>; or Ser-Ala-+-Ala-Lys <5>; hydrolyzed by serotypes BoNT/B <5>; D, F or G <5>; in vitro, in synaptosomes and in injected Aplysia neurons <5>; the term -+- depicts the points of cleavage	**6** , **13** , **14**	MW 8000 and MW 9000 <13>	**13**
Synaptobrevin + H2O	**Hydrolyzed synaptobrevin**		Clostridium barati	i.e. VAMP <5>; chicken <5>; or rat brain <5>; : synaptobrevin/VAMP-1 (VAMP-1 from chicken, #Clostridium botulinum,d#Clostridium barati,d#Clostridium butyricum# <5> or rat brain, #Clostridium botulinum,i#Clostridium barati,i#Clostridium butyricum# <4, 5> carrying Val76 instead	**5**	-	-

Synaptobrevin + H2O	**Hydrolyzed synaptobrevin**		Clostridium butyricum	of Gln76 is not hydrolyzed by serotype BoNT/B, #Clostridium botulinum,u#Clostridium barati,u#Clostridium butyricum# <4, 5>) <5>; and synaptobrevin/VAMP-2 <5>; highly specific neurotoxins <5>; serotype BoNT/B: cleavage at Ser-Gln-+-Phe-Glu (at the same site as the tetanus neurotoxin) <5>; or Gln-Lys-+-Leu-Ser <5>; or Ser-Ala-+-Ala-Lys <5>; hydrolyzed by serotypes BoNT/B <5>; D, F or G <5>; in vitro, in synaptosomes and in injected Aplysia neurons <5>; the term -+- depicts the points of cleavage	5	-	-
Synaptosome-associated protein + H2O	**Hydrolyzed synaptosome-associated protein**		Clostridium botulinum	i.e. SNAP 25, protein of presynaptic membrane <5>; MW 25000 <5>; native and recombinant protein <12>; highly specific neurotoxins <12>; serotype BoNT/A: cleavage at Gln197-Arg198 <12>; or Asn-Gln-+-Arg-Ala <5>; serotype BoNT/E: cleavage at Arg180-Ile181 <12>; or Asp-Arg-+-Ile-Met <5>; serotype BoNT/A and E <5,6,12>; in vitro, in isolated synaptosomes <5,12>; and in injected Aplysia neurons <5>; no substrate of serotype BoNT/G <15>; the term-+- depicts the points of cleavage	5 , 6 , 12	2 proteolytic fragments, MW 20500 and MW 3000 (serotype BoNT/E) or MW 22500 and MW 1000 (serotype BoNT/A)	12
Synaptosome-associated protein + H2O	**Hydrolyzed synaptosome-associated protein**		Clostridium barati	i.e. SNAP 25, protein of presynaptic membrane <5>; MW 25000 <5>; or Asn-Gln-+-Arg-Ala <5>; or Asp-Arg-+-Ile-Met <5>; serotype BoNT/A and E <5>; in vitro, in isolated synaptosomes <5>; and in injected Aplysia neurons <5>; the term-+- depicts the points of cleavage	5	2 proteolytic fragments, MW 20500 and MW 3000 (serotype BoNT/E) or MW 22500 and MW 1000 (serotype BoNT/A)	-
Synaptosome-associated protein + H2O	**Hydrolyzed synaptosome-associated protein**		Clostridium butyricum	i.e. SNAP 25, protein of presynaptic membrane <5>; MW 25000 <5>; or Asn-Gln-+-Arg-Ala <5>; or Asp-Arg-+-Ile-Met <5>; serotype BoNT/A and E <5>; in vitro, in isolated synaptosomes <5>; and in injected Aplysia neurons <5>; the term-+- depicts the points of cleavage	5	2 proteolytic fragments, MW 20500 and MW 3000 (serotype BoNT/E) or MW 22500 and MW 1000 (serotype BoNT/A)	-

Synaptosome-associated protein + H2O	**Hydrolyzed synaptosome-associated protein**		Clostridium sp.	i.e. SNAP 25, protein of presynaptic membrane <13>; serotype BoNT/A and E <6,13>; the term-+- depicts the points of cleavage	6 , 13		2 proteolytic fragments, MW 20500 and MW 3000 (serotype BoNT/E) or MW 22500 and MW 1000 (serotype BoNT/A)	-
Syntaxin + H2O	**?**		Clostridium botulinum	serotype BoNT/C <5,6>; in vitro, in synaptosomes and in injected Aplysia neurons <5>; no substrate of serotype BoNT/G <15>	5 , 6		-	-
Syntaxin + H2O	**?**		Clostridium barati	serotype BoNT/C <5>; in vitro, in synaptosomes and in injected Aplysia neurons <5>	5		-	-
Syntaxin + H2O	**?**		Clostridium butyricum	serotype BoNT/C <5>; in vitro, in synaptosomes and in injected Aplysia neurons <5>	5		-	-
Syntaxin + H2O	**?**		Clostridium sp.	serotype BoNT/C <6>	6		-	-

NATURAL SUBSTRATE	NATURAL PRODUCT	REACTION DIAGRAM	ORGANISM	COMMENTARY SUBSTRATE	LITERATURE **(Substrate)**	COMMENTARY PRODUCT	LITERATURE **(Product)**	ORGANISM **(Product)**
Neuroexocytosis multi-subunit complex + H2O	-		Clostridium botulinum	involved in limited hydrolysis of proteins of the neuroexocytosis apparatus, blocks release of neurotransmitter acetylcholine at neuromuscular junction <5>; causing flaccid paralysis, in contrast to spastic paralysis caused by EC 3.4.24.68, three functionally distinct domains: domain L blocks neuroexocytosis, domain HN governs cell penetration, domain HC responsible for neurospecific binding <5,6>; neurotoxin binds specifically to nerve cells, botulin neurotoxin-receptors are located on the motor neuron plasmalemma at neuromuscular junctions, neurotoxin binds via protein and lipid interaction, after binding it is internalized inside vesicles of unknown nature	5 , 6	-	-	-

Neuroexocytosis multi-subunit complex + H2O	-		Clostridium barati	involved in limited hydrolysis of proteins of the neuroexocytosis apparatus, blocks release of neurotransmitter acetylcholine at neuromuscular junction <5>; causing flaccid paralysis, in contrast to spastic paralysis caused by EC 3.4.24.68, three functionally distinct domains: domain L blocks neuroexocytosis, domain HN governs cell penetration, domain HC responsible for neurospecific binding <5>; neurotoxin binds specifically to nerve cells, botulin neurotoxin-receptors are located on the motor neuron plasmalemma at neuromuscular junctions, neurotoxin binds via protein and lipid interaction, after binding it is internalized inside vesicles of unknown nature	**5**	-	-	-
Neuroexocytosis multi-subunit complex + H2O	-		Clostridium butyricum	involved in limited hydrolysis of proteins of the neuroexocytosis apparatus, blocks release of neurotransmitter acetylcholine at neuromuscular junction <5>; causing flaccid paralysis, in contrast to spastic paralysis caused by EC 3.4.24.68, three functionally distinct domains: domain L blocks neuroexocytosis, domain HN governs cell penetration, domain HC responsible for neurospecific binding <5>; neurotoxin binds specifically to nerve cells, botulin neurotoxin-receptors are located on the motor neuron plasmalemma at neuromuscular junctions, neurotoxin	**5**	-	-	-

				binds via protein and lipid interaction, after binding it is internalized inside vesicles of unknown nature				
Neuroexocytosis multi-subunit complex + H2O	-		Clostridium sp.	causing flaccid paralysis, in contrast to spastic paralysis caused by EC 3.4.24.68, three functionally distinct domains: domain L blocks neuroexocytosis, domain HN governs cell penetration, domain HC responsible for neurospecific binding <6>; neurotoxin binds specifically to nerve cells, botulin neurotoxin-receptors are located on the motor neuron plasmalemma at neuromuscular junctions, neurotoxin binds via protein and lipid interaction, after binding it is internalized inside vesicles of unknown nature	**6**	-	-	-
Synaptobrevin + H2O	-		Clostridium botulinum	i.e. VAMP <5,6,12>; synaptic vesicle-associated membrane protein, neurotoxin responsible for human and animal botulism <12>	**4** , **5** , **6** , **12**	-	-	-
Synaptobrevin + H2O	-		Clostridium barati	i.e. VAMP <5>	**5**	-	-	-
Synaptobrevin + H2O	-		Clostridium butyricum	i.e. VAMP <5>	**5**	-	-	-
Synaptobrevin + H2O	-		Clostridium sp.	i.e. VAMP <6>	**6**	-	-	-
Synaptosome-associated protein + H2O	-		Clostridium botulinum	i.e. SNAP 25, protein of presynaptic membrane	**5**	-	-	-
Synaptosome-associated protein + H2O	-		Clostridium barati	i.e. SNAP 25, protein of presynaptic membrane	**5**	-	-	-
Synaptosome-associated protein + H2O	-		Clostridium butyricum	i.e. SNAP 25, protein of presynaptic membrane	**5**	-	-	-
Synaptosome-associated protein + H2O	-		Clostridium sp.	i.e. SNAP 25, protein of presynaptic membrane	**13**	-	-	-

COFACTOR	ORGANISM	COMMENTARY	LITERATURE	IMAGE
No entries in this field				

METAL IONS	ORGANISM	COMMENTARY	LITERATURE
More	Clostridium botulinum	no involvement of cobalt, copper, iron, manganese or nickel, atomic absorption spectroscopy	1
More	Clostridium sp.	no involvement of cobalt, copper, iron, manganese or nickel, atomic absorption spectroscopy	14
Zinc	Clostridium botulinum	zinc-dependent endopeptidase (serotype BoNT/B, #Clostridium botulinum,t#Clostridium sp.# <4, 6>) <4,6,12,15>; atom absorption spectroscopy <1,5,6>; : 1 atom of zinc per molecule botulinum neurotoxin (MW 150000, of serotypes A, B and E, each in 2-chain form, #Clostridium botulinum# <1>), bound to light chain (i.e. L-chain) <5>; the L-chain of BoNT/B is a form of zinc-endopeptidase <6>; 0.8-1 gatom zinc/mol neurotoxin <6>; contains zinc binding motif of metalloendopeptidases His-Glu-X-X-His <1,5,15>; or His223-Glu-Leu-Ile-His-X-X-His230 <10>; activation requires reduction of interchain disulfide bond <4,15>	1, 4, 5, 6, 10, 12, 15
Zinc	Clostridium barati	atom absorption spectroscopy <5>; : 1 atom of zinc per molecule botulinum neurotoxin (MW 150000, of serotypes A, B and E, each in 2-chain form, #Clostridium botulinum# <1>), bound to light chain (i.e. L-chain) <5>; contains zinc binding motif of metalloendopeptidases His-Glu-X-X-His <5>	5
Zinc	Clostridium butyricum	atom absorption spectroscopy <5>; : 1 atom of zinc per molecule botulinum neurotoxin (MW 150000, of serotypes A, B and E, each in 2-chain form, #Clostridium botulinum# <1>), bound to light chain (i.e. L-chain) <5>; contains zinc binding motif of metalloendopeptidases His-Glu-X-X-His <5>	5
Zinc	Clostridium sp.	zinc-dependent endopeptidase (serotype BoNT/B, #Clostridium botulinum,n#Clostridium sp.# <4, 6>) <6,13,14>; atom absorption spectroscopy <6,14>; : 1 atom of zinc per molecule botulinum neurotoxin (MW 150000, of serotypes A, B and E, each in 2-chain form, #Clostridium botulinum# <1>), bound to light chain (i.e. L-chain) <14>; the L-chain of BoNT/B is a form of zinc-endopeptidase <6>; 0.8-1 gatom zinc/mol neurotoxin <6>	6, 13, 14

INHIBITORS	ORGANISM	COMMENTARY	LITERATURE	IMAGE
1,10-Phenanthroline	Clostridium botulinum	-	1, 15	2D-image
1,10-Phenanthroline	Clostridium sp.	r, Zn2+ restores <14>	14	2D-image
Ala-Ser-Gln-Phe-Glu-Thr-Ser	Clostridium botulinum	synthetic peptide containing cleavage site of synaptobrevin, inhibits toxin action on buccal ganglion of Aplysia californica, serotype BoNT/B, not A or E	4	2D-image
Captopril	Clostridium botulinum	serotype BoNT/B <4>	4, 5, 15	2D-image
Captopril	Clostridium barati	-	5	2D-image
Captopril	Clostridium butyricum	-	5	2D-image
Captopril	Clostridium sp.	-	13, 14	2D-image
Dipicolinic acid	Clostridium botulinum	-	1	2D-image
EDTA	Clostridium botulinum	r, Zn2+ restores <1>; serotype BoNT/B <4>	1, 4, 15	2D-image
EDTA	Clostridium sp.	r, Zn2+ restores <14>	13, 14	2D-image
Gln-Phe-Glu-Thr	Clostridium botulinum	synthetic peptide containing cleavage site of synaptobrevin, inhibits toxin action on buccal ganglion of Aplysia californica, serotype BoNT/B, not A or E	4	2D-image

ACTIVATING COMPOUND	ORGANISM	COMMENTARY	LITERATURE	IMAGE
Proteases	Clostridium botulinum	activation by rapid cleavage of MW 150000 polypeptide chain and generation of active di-chain neurotoxin <5,6>; bacterial or tissue proteases <5>	5,6	-
Proteases	Clostridium barati	activation by rapid cleavage of MW 150000 polypeptide chain and generation of active di-chain neurotoxin <5>; bacterial or tissue proteases <5>	5	-

Proteases	Clostridium butyricum	activation by rapid cleavage of MW 150000 polypeptide chain and generation of active di-chain neurotoxin <5>; bacterial or tissue proteases <5>	5	-
Proteases	Clostridium sp.	activation by rapid cleavage of MW 150000 polypeptide chain and generation of active di-chain neurotoxin <6>	6	-

KM VALUE [mM] KM VALUE [mM] Maximum SUBSTRATE ORGANISM COMMENTARY LITERATURE IMAGE

No entries in this field

Ki VALUE [mM] Ki VALUE [mM] Maximum INHIBITOR ORGANISM COMMENTARY LITERATURE IMAGE

No entries in this field

TURNOVER NUMBER TURNOVER NUMBER MAXIMUM SUBSTRATE ORGANISM COMMENTARY LITERATURE IMAGE

No entries in this field

SPECIFIC ACTIVITY [µM/min/mg] SPECIFIC ACTIVITY MAXIMUM ORGANISM COMMENTARY LITERATURE

No entries in this field

pH OPTIMUM pH MAXIMUM ORGANISM COMMENTARY LITERATURE

No entries in this field

pH RANGE pH RANGE MAXIMUM ORGANISM COMMENTARY LITERATURE

No entries in this field

TEMPERATURE OPTIMUM	TEMPERATURE OPTIMUM MAXIMUM	ORGANISM	COMMENTARY	LITERATURE
37	-	Clostridium botulinum	assay at	4 , 6 , 12 , 15
37	-	Clostridium sp.	assay at	6 , 13 , 14

TEMPERATURE RANGE TEMPERATURE MAXIMUM ORGANISM COMMENTARY LITERATURE

No entries in this field

SOURCE TISSUE ORGANISM COMMENTARY LITERATURE

No entries in this field

LOCALIZATION	ORGANISM	COMMENTARY	GeneOntology No.	LITERATURE
cytosol	Clostridium botulinum	accumulates until bacterial lysis	GO:0005829	5 , 6
cytosol	Clostridium barati	accumulates until bacterial lysis	GO:0005829	5
cytosol	Clostridium butyricum	accumulates until bacterial lysis	GO:0005829	5
cytosol	Clostridium sp.	accumulates until bacterial lysis	GO:0005829	6

ACCESSION CODE ENTRY NAME ORGANISM NO. OF AA MOLECULAR WEIGHT[Da] SOURCE Sequence

No entries in this field

PDB	ORGANISM
1E1H, download	Clostridium botulinum
1EPW, download	Clostridium botulinum
1F31, download	Clostridium botulinum
1F82, download	Clostridium botulinum
1F83, download	Clostridium botulinum
1FQH, download	Clostridium botulinum
1G9A, download	Clostridium botulinum

1G9B, download Clostridium botulinum

1G9C, download Clostridium botulinum

1G9D, download Clostridium botulinum

1I1E, download Clostridium botulinum

3BTA, download Clostridium botulinum

MOLECULAR WEIGHT	MOLECULR WEIGHT MAXIMUM	ORGANISM	COMMENTARY	LITERATURE
155000	-	Clostridium botulinum	Clostridium botulinum, serotype BoNT/B, calculated from amino acid sequence	8
152000	-	Clostridium botulinum	Clostridium botulinum, serotype BoNT/E, calculated from amino acid sequence	8
150000	-	Clostridium botulinum	Clostridium botulinum, serotype BoNT/A, SDS-PAGE, calculated from amino acid sequence	8
149500	-	Clostridium botulinum	Clostridium botulinum, serotype BoNT/A, calculated from nucleotide sequence	9
149400	-	Clostridium botulinum	Clostridium botulinum, serotype BoNT/A, calculated from nucleotide sequence	10
148700	-	Clostridium botulinum	Clostridium botulinum, serotype BoNT/C1, calculated from nucleotide sequence	3
146900	-	Clostridium botulinum	Clostridium botulinum, serotype BoNT/D, calculated from nucleotide sequence	2
additional information	-	Clostridium botulinum	amino acid content <8>; comparison of amino acid sequences of H- and L-chains of serotypes A, B and E <8>; comparison of amino acid sequences of botulinum serotype BoNT/A and tetanus neurotoxin <9,10>; amino acid sequence similarity of clostridial neurotoxins	8 , 9 , 10
additional information	-	Clostridium sp.	amino acid content; comparison of amino acid sequences of H- and L-chains of serotypes A, B and E; comparison of amino acid sequences of botulinum serotype BoNT/A and tetanus neurotoxin; amino acid sequence similarity of clostridial neurotoxins <14>	14

SUBUNITS	ORGANISM	COMMENTARY	LITERATURE
Dimer	Clostridium botulinum	1 * 50000 + 1 * 102000, Clostridium botulinum, serotype BoNT/E, calculated from amino acid sequence, 1 * 51000 + 1 * 104000, Clostridium botulinum, serotype BoNT/B, calculated from amino acid sequence, 1 * 53000 + 1 * 97000, Clostridium botulinum, serotype BoNT/A, calculated from amino acid sequence	8
More	Clostridium botulinum	synthesized as single-chain polypeptide of about MW 150000, proteolytic activation yields 2-chain neurotoxin with N-terminal light (MW 50000) and C-terminal heavy chains (MW 100000) connected by single disulfide bonds <2,3,6>; serotype BoNT/E: single-chain polypeptide, serotype BoNT/B: mixture of single- and 2-chain molecules, serotype BoNT/A: 2-chain molecule <8>	2 , 3 , 6 , 8
More	Clostridium sp.	synthesized as single-chain polypeptide of about MW 150000, proteolytic activation yields 2-chain neurotoxin with N-terminal light (MW 50000) and C-terminal heavy chains (MW 100000) connected by single disulfide bonds <6>; serotype BoNT/E: single-chain polypeptide, serotype BoNT/B: mixture of single- and 2-chain molecules, serotype BoNT/A: 2-chain molecule	6

POSTTRANSLATIONAL MODIFICATION ORGANISM COMMENTARY LITERATURE

No entries in this field

Crystallization/COMMENTARY ORGANISM LITERATURE

No entries in this field

pH STABILITY pH STABILITY MAXIMUM ORGANISM COMMENTARY LITERATURE

No entries in this field

TEMPERATURE STABILITY TEMPERATURE STABILITY MAXIMUM ORGANISM COMMENTARY LITERATURE

No entries in this field

GENERAL STABILITY ORGANISM LITERATURE

No entries in this field

ORGANIC SOLVENT ORGANISM COMMENTARY LITERATURE

No entries in this field

OXIDATION STABILITY	ORGANISM	LITERATURE
-	Clostridium botulinum	6

STORAGE STABILITY	ORGANISM	COMMENTARY	LITERATURE
-80°C, in 10 mM HEPES buffer, pH 7.2, 50 mM NaCl, after freezing in liquid N2, stable	Clostridium botulinum	-	6

Purification/COMMENTARY	ORGANISM	LITERATURE
serotypes BoNT/A to F	Clostridium sp.	11
serotypes BoNT/A, B, E (and their H-chain and L-chain <8>) <6,8>; C, D, F <6>	Clostridium botulinum	6 , 8

Cloned/COMMENTARY	ORGANISM	LITERATURE
Clostridium botulinum <2,3>; serotypes BoNT/A (3 fragments encompassing the structural gene <9>) <9,10>; C1 <2,3>; or D <2>; expressed in Escherichia coli TG1 <9>	Clostridium botulinum	2 , 3 , 9 , 10

ENGINEERING ORGANISM COMMENTARY LITERATURE

No entries in this field

Renatured/COMMENTARY ORGANISM LITERATURE

No entries in this field

APPLICATION ORGANISM COMMENTARY LITERATURE

No entries in this field

DISEASE	TITLE OF PUBLICATION	LINK TO PUBMED
Blepharoptosis	-	PubMed
Blepharoptosis	-	PubMed
Botulism	-	PubMed
Botulism	-	PubMed
Botulism, Infantile	-	PubMed
Botulism, Infantile	-	PubMed
Nerve paralysis	-	PubMed
Nerve paralysis	-	PubMed
Nystagmus, Pathologic	Treatment of acquired nystagmus with botulinum neurotoxin A.	PubMed

REF.	AUTHORS	TITLE	JOURNAL	VOL.	PAGES	YEAR	ORGANISM	COMMENTARY	LINK TO PUBMED
1	Schiavo, G.; Rossetto, O.; Santucci, A.; DasGupta, B.R.; Montecucco, C.	**Botulinum neurotoxins are zinc proteins**	J. Biol. Chem.	267	23479-23483	1992	Clostridium botulinum	-	PubMed
2	Binz, T.; Kurazono, H.; Popoff, M.R.; Eklund, M.W.; Sakaguchi, G.; Kozaki, S.; Krieglstein, K.; Henschen, A.; Gill, D.M.; Niemann, H.	**Nucleotide sequence of the gene encoding Clostridium botulinum neurotoxin type D**	Nucleic Acids Res.	18	5556	1990	Clostridium botulinum	-	PubMed

3	Hauser, D.; Eklund, M.W.; Kurazono, H.; Binz, T.; Niemann, H.; Gill, D.M.; Boquet, P.; Popoff, M.R.	**Nucleotide sequence of Clostridium botulinum C1 neurotoxin**	Nucleic Acids Res.	18	4924	1990	Clostridium botulinum	-	PubMed
4	Schiavo, G.; Benfenati, F.; Poulain, B.; Rossetto, O.; Polverino de Laureto, P.; DasGupta, B.R.; Montecucco, C.	**Tetanus and botulinum-B neurotoxins block neurotransmitter release by proteolytic cleavage of synaptobrevin [see comments]**	Nature	359	832-835	1992	Clostridium botulinum	-	PubMed
5	Montecucco, C.; Schiavo, G.	**Mechanism of action of tetanus and botulinum neurotoxins**	Mol. Microbiol.	13	1-8	1994	Clostridium botulinum, Clostridium barati, Clostridium butyricum	review	PubMed
6	Schiavo, G.; Montecucco, C.	**Tetanus and botulism neurotoxins: isolation and assay**	Methods Enzymol.	248	643-652	1995	Clostridium botulinum, Clostridium sp.	review	PubMed
7	Eisel, U.; Jarusch, W.; Goretzki, K.; Henschen, A.; Engels, J.; Weller, U.; Hudel, M.; Habermann, E.; Niemann, H.	**Tetanus toxin: primary structure, expression in E. coli, and homology with botulinum toxins**	EMBO J.	5	2495-2502	1986	Clostridium botulinum	-	PubMed
8	Saathyamoorthy, V.; DasGupta, B.R.	**Separation, purification, partial characterization and comparison of the heavy and light chains of botulinum neurotoxin types A, B, and E**	J. Biol. Chem.	260	10461-10466	1985	Clostridium botulinum	-	PubMed
9	Thompson, D.E.; Brehm, J.K.; Oultram, J.D.; Swinfield, T.-J.; Shone, C.C.; Atkinson, T.; Melling, J.; Minton, N.P.	**The complete amino acid sequence of the Clostridium botulinum type A neurotoxin, deduced by nucleotide sequence analysis of the encoding gene**	Eur. J. Biochem.	189	73-81	1990	Clostridium botulinum	-	PubMed
10	Binz, T.; Kurazono, H.; Wille, M.; Frevert, J.; Wernars, K.; Niemann, H.	**The complete sequence of botulinum neurotoxin type A and comparison with other clostridial neurotoxins**	J. Biol. Chem.	265	9153-9158	1990	Clostridium botulinum	-	PubMed
11	Simpson, L.L.; Schmidt, J.J.; Middlebrook, J.L.	**Isolation and characterization of the botulinum neurotoxins**	Methods Enzymol.	165	76pp	1988	Clostridium sp.	-	-
12	Schiavo, G.; Santucci, A.; DasGupta, B.R.; Mehta, P.P.; Jontes, J.; Benfenati, F.; Wilson, M.C.; Montecucco, C.	**Botulinum neurotoxins serotypes A and E cleave SNAP-25 at distinct COOH-terminal peptide bonds**	FEBS Lett.	335	99-103	1993	Clostridium botulinum	-	PubMed
13	Schiavo, G.; Rossetto, O.; Catsicas, S.; Polverino de Laureto, P.; DasGupta, B.R.; Benfenati, F.; Montecucco, C.	**Identification of the nerve terminal targets of botulinum neurotoxin serotypes A, D, and E**	J. Biol. Chem.	268	23784-23787	1993	Clostridium sp.	-	PubMed
14	Schiavo, G.; Shone, C.C.; Rossetto, O.; Alexander, F.C.G.; Montecucco, C.	**Botulinum neurotoxin serotype F is a zinc endopeptidase specific for VAMP/synaptobrevin**	J. Biol. Chem.	268	11516-11519	1993	Clostridium sp.	-	PubMed
15	Schiavo, G.; Malizio, C.; Trimble, W.S.; Polverino de Laureto, P.; Milan, G.;	**Botulinum G neurotoxin cleaves VAMP/synaptobrevin at a**	J. Biol.	269	20213-	1994	Clostridium	-	PubMed

Sugiyama, H.; Johnson, E.A.; Montecucco, C.	**single Ala-Ala peptide bond**	Chem.	20216	botulinum

LINKS TO OTHER DATABASES (specific for EC-Number 3.4.24.69)

ExPASy

Online Mendelian Inheritance in Man

KEGG

NCBI: **PubMed**, **Protein**, **Nucleotide**, **Structure**, **Genome**, **OMIM**, **Domains**

IUBMB Enzyme Nomenclature

WIT database

EMP Project

PDB database(3D structure)

PROSITE Database of protein families and domains

SYSTERS

Protein Mutant Database